Extremal factors of different nature thus caused changes of a similar character in the cyclic AMP system. The general biological significance of cyclic AMP in the mechanism of neurohumoral regulatory influences and the integration of cellular metabolism suggests that universality of this response reflects one of the central adaptive mechanisms of the cell and of the organism as a whole.

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ENERGY POTENTIAL OF THE CEREBRAL CORTEX IN THE PREAGONAL AND RESUSCITATION PERIODS AFTER ACUTE BLOOD LOSS

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In experiments on dogs the ATP concentration fell (by 38%) and the ADP and AMP concentrations rose by 121 and 875%, respectively, in the cortical gray matter in the preagonal period after hypovolemic hypotension for 4 h. Reflecting these changes, the energy potential fell from 0.931 to 0.736 ($P < 0.05$). In the early and late postresuscitation period the concentrations of these metabolites and the level of the energy potential were the same as initially.

KEY WORDS: energy potential; cerebral cortex; hypovolemic hypotension; postresuscitation period.

It was shown previously that profound degenerative changes develop in the cerebral cortex in the late postresuscitation period after massive blood loss and prolonged hypotension, as the result of a disturbance of structural metabolism and proteolysis [3].

Investigation of the energy metabolism under these conditions is particularly important, for impairment of the energy supply is known to be a trigger factor in the disturbance of brain nutrition [1, 2, 8]. Meanwhile the study of the energy state of the CNS in preagonal states developing after prolonged hypotension caused by blood loss are not homogeneous and they apply mainly to acute hypoxia and not to the postresuscitation period [7, 13].

The object of this investigation was to study the energy potential of the adenine–nucleotide system of the cerebral cortex (the gray matter) in the preagonal state after hypovolemic hypotension for 4 h, and also in the early and late postresuscitation period.

EXPERIMENTAL METHOD

Experiments were carried out on 13 adult dogs of both sexes. After trimeperidine premedication (10 mg/kg) and under extensive local anesthesia rapid bleeding was carried out for a period of 3-5 min from the femoral artery, reducing the blood pressure to 40 mm Hg, at which level it was maintained for 4 h.

Toward the end of the period of hypotension the mean blood loss was 40 ± 5 ml/kg body weight. The blood pressure was restored by intraarterial reinfusion of the blood in small doses (50-150 ml) into the femor-

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TABLE 1. Changes in ATP, ADP, and AMP Concentrations and Energy Potential of Cerebral Cortex of Dogs in Preagonal and Postresuscitation Periods (M ± m)

Parameter	Control	Preagonal state	Recovery period	
			1 h	3–4 months
ATP, μmoles/g	2,74±0,10 (4)	1,70±0,05*(3)	2,51±0,08 (3)	2,75±0,08 (3)
ADP, μmoles/g	0,34±0,02 (4)	0,75±0,03*(3)	0,29±0,05 (3)	0,28±0,05 (3)
AMP, μmoles/g	0,04±0,005 (4)	0,35±0,05*(3)	0,05±0,02 (3)	0,06±0,01 (3)
Energy potential	0,931±0,001 (4)	0,736±0,008*(3)	0,933±0,030 (3)	0,936±0,007 (3)

Legend. 1) Number of experiments in parentheses.
*Results differing significantly ($P < 0.05$) from control.

al artery. After replacement of the lost blood the animals were given dextran (25-30 ml/kg) by intravenous drip infusion.

Biochemical investigations were undertaken during acute experiments on control animals (group 1, four dogs), at the end of the 4th hour of hypotension (group 2, three dogs), 1 h after the beginning of resuscitation measures (group 3, three dogs), and during the 3rd-4th months of the postresuscitation period (group 4, three dogs).

The skull was trephined under superficial thiopental anesthesia. The brain tissue was frozen in situ with liquid nitrogen through the burr hole. Pieces of frozen tissue were cut into small pieces and extracted with perchloric acid. The concentrations of ATP, ADP, and AMP in the extract were determined by Bergmeyer's enzymic method [5] on the SF-4A spectrophotometer at 366 nm. The energy state of the tissue of the gray matter was assessed as the energy potential of adenine nucleotides, calculated by the following equation [6]:

$$\text{Energy potential} = \frac{\text{ATP} + 0.5\text{ADP}}{\text{ATP} + \text{ADP} + \text{AMP}}.$$

EXPERIMENTAL RESULTS

As the results in Table 1 show, the ATP concentration in the cortical gray matter of the dogs at the end of the 4th hour of hypovolemic hypotension (the preagonal state) fell by 38% ($P < 0.05$), whereas the ADP and AMP concentrations rose by 121 and 875%, respectively. The energy potential of the cortical gray matter decreased regularly.

The concentrations of ATP, ADP, and AMP and also the energy potential in the cortex were restored 1 h after resuscitation.

In the late postresuscitation period the concentration of these metabolites was the same as initially.

Previous investigations of cortical anaerobic metabolism during prolonged hypovolemic hypotension have demonstrated a marked increase in the lactic acid concentration [9] and a decrease in the potassium concentration and pseudocholinesterase activity [13]. In prolonged hypotention caused by massive blood loss, hypoxia inhibits oxidative phosphorylation and the quantity of ATP formed is insufficient to maintain cell function [7, 13].

Under the conditions of decompensated blood loss and clinical death, as was shown previously, profound disturbances of carbohydrate and phosphate metabolism are evidence that the glycolytic pathway cannot maintain the resynthesis of high-energy phosphorus compounds [2, 4, 11, 12]. At the same time, total loss of creatine phosphate was discovered.

The regular decrease in the ATP concentration and the increase in the ADP and AMP concentrations in the preagonal period, expressed as a reduction in the cerebral cortical energy potential, points to cerebral hypoxia in this state and a disturbance of the mechanisms of autoregulation of the blood supply to the brain.

Reinfusion of blood after 1 h restored the energy potential of the cortical gray matter and so abolished the cerebral hypoxia. The energy potential of the cerebral cortex remained at its initial level for 3-4 months of the postresuscitation period despite profound disturbances of the structural metabolism and regions of destruction [3]. The results indicate that early restoration of the normal energy potential of the adenine–nucleotide system in the cortical gray matter cannot prevent the development of degenerative changes characteristic of the postresuscitation state.

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EFFECT OF DISSEMINATED NECROSIS OF THE HEART ON UPTAKE OF RADIOACTIVE PRECURSORS INTO RNA OF INTERNAL MITOCHONDRIAL MEMBRANES OF THE RAT MYOCARDIUM

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The role of the internal mitochondrial membranes of the rat myocardium as the site of uptake of radioactive precursors into mitochondrial RNA was studied. The kinetics of the changes in specific RNA activity of the internal mitochondrial membranes of the myocardium was found to differ in vivo and in vitro. Necrosis of the myocardium, in experiments in vivo and in vitro, caused significant changes in the specific RNA activity of the mitochondrial membranes in the same direction.

KEY WORDS: disseminated necrosis of the heart; RNA synthesis; internal mitochondrial membranes; isoproterenol.

The internal membranes of the mitochondria are the site of incorporation of radioactive precursors of nucleic acids and proteins [6, 9]. Necrosis of the heart has been shown to have a considerable effect on protein synthesis in the internal mitochondrial membranes of the rat myocardium [3, 4]. It is not known, however, whether this effect extends only to the activity of the protein molecule already synthesized or whether the resulting ischemia is capable of producing changes in metabolism at a lower level of integration of the organelle, in the reaction sequence DNA—RNA—mitochondrial protein.

To investigate this problem RNA synthesis was studied in the internal mitochondrial membranes of the myocardium in intact rats and in rats with disseminated necrosis of the heart.

EXPERIMENTAL METHOD

Male Wistar rats weighing 250-280 g were used. Myocardial necrosis was induced by subcutaneous injection of the sympathomimetic agent isoproterenol sulfate [1, 3, 4]. The appearance of necrotic foci in the myocardium was monitored by periodic recording of the ECG. Investigations were carried out both in vitro and in vivo.

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