GENERAL PATHOLOGY AND PATHOPHYSIOLOGY

Effect of Neuromedin on Activity of Lactate Dehydrogenase in Mitochondrial Fraction of the Brain in Rats with Thermal Injury

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We studied enzyme systems (lactate dehydrogenase) of mitochondria in cerebral nerve cells in experimental encephalopathy developing after thermal injury. In animals receiving neuromedin at the early terms after injury, the ratio of forward to reverse lactate dehydrogenase reactions significantly increased over the first day after injury and returned to normal on day 7.

Key Words: *Mitochondrial lactate dehydrogenase; encephalopathy; burns*

Encephalopathy, the most incident clinical form of cerebral pathology in thermal injury [4] during the acute period, develops due to extreme excitation, hypoxia, and toxicosis (at later stages). According to modern notions, hypoxia of any kind is a pathological process determined by dysfunction of mitochondrial enzymes [1]. However, pathogenesis of neuronal damage in thermal injury, mechanisms of initiation of these changes, and possible ways of their targeted prophylaxis remain little studied.

Here we studied the effects of neuromedins on regulation of lactate dehydrogenase (LDH) activity in the mitochondrial fraction from the brain of rats with experimental thermal injury.

MATERIALS AND METHODS

Male Wistar rats were narcotized with ether and burn injury was inflicted on depilated skin (contact thermal injury, 20% body surface, grade III A and B). Amiridin (neuromedin, 0.2 mg in 1 ml physiological saline) was injected intraperitoneally 1 h after injury and then daily for 7 days. The animals were observed for 7 days. Samples for enzyme assay were taken 1 and 24 h and 3 and 7 days after infliction of experimental burn and on day 3, 5, and 7 of treatment. The animals were decapitated and the brain was removed in cold. Mitochondrial fraction of the brain was isolated by differential centrifugation [3], LDH activity in forward and reverse reactions was measured [2].

The data were processed statistically using parametric methods, the means and standard deviations were calculated, Student *t* test was applied.

RESULTS

In intact animals, LDH activity for conversion of lactate into pyruvate was higher by 2.3 times than in the reverse reaction (Table 1). In animals with thermal injury, activity of mitochondrial LDH in the forward reaction gradually decreased to 50% of the control (Table 1).

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TABLE 1. Activity of LDH in Mitochondrial Fraction from the Brain of Rats with Experimental Thermal Injury (nmol NADH/min×mg protein)

Parameter	Control (n=10)	Time of observation			
		1 h (n=10)	24 h (n=10)	3 days (n=10)	7 days (n=10)
Forward LDH reaction	105.26±7.69	133.52±5.52*	70.466±9.100*	67.74±4.70*	48.81±3.61*
Reverse LDH reaction	45.81±3.03	107.12±1.64*	131.80±7.81*	90.44±3.13*	101.66±1.70*
Forward LDH/reverse LDH	2.3	1.2	0.5	0.7	0.5

Note. Here and in Table 2: *p<0.05 compared to control group.

TABLE 2. Activity of LDH in Mitochondrial Fraction from the Brain of Rats with Experimental Thermal Injury Treated with Neuromedin (nmol NADH/min×mg protein)

Parameter	Control	Time of observation		
		3 days	5 days	7 days
Forward LDH reaction	105.26±7.69	165.23±2.46*	132.98±3.52*	238.08±0.85*
Reverse LDH reaction	45.81±3.03	135.68±1.62*	189.82±1.93*	96.81±0.13*
Forward LDH/reverse LDH	2.3	1.2	0.7	2.5

Activity of mitochondrial LDH in the reverse reaction gradually increased to day 7. These changes attest to activation of anaerobic glycolysis in the brain of animals with thermal injury, which is primarily related to changes in activity of mitochondrial LDH playing a role of enzyme coordinators of energy metabolism in nerve cells.

In animals receiving neuromedin, the ratio of forward to reverse LDH reaction in the mitochondrial fraction decreased only on days 3 and 5. However, on day 7 this ratio was restored to a level observed in the control group (Table 2). Activity of mitochondrial LDH in both reactions increased by more than 2 times (Table 2). It can be hypothesized that neuromedin activates energy metabolism in cells. The anticholinesterase effect of neuromedin leads to accumulation of acetylcholine in synaptosomes and elevation of the cholinergic potential of the nerve system. This, in combination with the effect of the drug on calcium channels leads to intensification of mitochondrial function in nerve cells. These processes modulate activity of mitochondrial LDH in rat brain under the effect of neuromedin in the posttraumatic period.

Thus, the results of this study confirm the leading role of hypoxia in the pathogenesis of brain pathology in thermal injury and the possibility of prophylactic modulation of these pathological processes.

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