ROLE OF LIPID PEROXIDATION IN BRAIN NEURON DAMAGE DURING AND AFTER ISCHEMIA

V. V. Semchenko, L. V. Poluéktov, and V. D. Konvai

UDC 616.831-005.4-06:616.831-091.81-092

KEY WORDS: liquid peroxidation; neuron; brain; ischemia; postischemic period.

The mechanism of ischemic damage to the structure and function of neurons has received little study, especially in the early stages [1, 4]. One factor triggering this process may be an intensification of lipid peroxidation (LPO) in the brain during ischemia and in the early recovery period. The aim of the present investigation was to test this hypothesis.

EXPERIMENTAL METHOD

Experiments were carried out on 36 male albino rats weighing 180-220 g under ether anesthesia; nine of the animals were controls. The model of ischemia consisted of clinical death lasting 5 min, produced by blood loss through the external iliac artery, followed by resuscitation by a modified Negovskii's method. The brain was fixed intravitally in liquid nitrogen at the end of ischemia and after 30 min and 24 h of the recovery period (six animals at each time). The antioxidant activity of lipids [9] and the concentrations of diene conjugates [10] and malonic dialdehyde (MDA) [5] were determined in tissue from the cerebral hemispheres. For electron microscopy the brain was perfused intravitally with a mixture of 4% paraform and 1% glutaraldehyde in phosphate buffer, pH 7.4 (three animals at each time). Pieces of cortex from the sensomotor area were treated in the usual way for survey multimicroscopy (embedding in Araldite, ultrathin sections stained with uranyl acetate and lead citrate). The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

During the period of ischemia the antioxidant activity of brain tissue lipids fell by 32.5% compared with the control. It remained at the same level 30 min after the beginning of ischemia. After 24 h only a tendency was observed toward recovery of this parameter (Table 1). The concentrations of diene conjugates and MDA in the brain tissue increased during ischemia by 22.5 and 53.5% respectively. This increase reached an even higher level after 30 min of the postischemic period. After 24 h the concentrations of diene conjugates remained high in the majority of animals, whereas the MDA concentration was low.

Mitochondria and the rough endoplasmic reticulum of the neurons were subjected to ultrastructural analysis, as the organelles most sensitive to hypoxia [1]. During ischemia, moderate swelling of mitochondria with focal destruction of their cristae, local lysis of the tubules of the rough endoplasmic reticulum, and an uneven widening of their lumen were observed in a small group of nerve cells. The number of nerve cells with structurally damaged mitochondria, with focal or, less frequently, subtotal lysis of the Nissl's substance, and with dilated tubules of the rough endoplasmic reticulum was increased 30 min after the beginning of ischemia. On the whole, however, these changes could be described as moderate. After 24 h various degrees of severity of destructive and metabolic changes in the organelles could be seen in most cerebral cortical neurons (Fig. 1).

The decrease in antioxidant activity in brain tissue at the end of ischemia is evidence of accumulation of superoxide radicals, capable of interacting with hydrogen peroxide to form hydroxyl radicals inducing LPO of unsaturated membrane fatty acids [8], in the brain. The level of antioxidant activity correlates negatively with the free radical concentration [7]. An increase in the concentration of lipid hydroperoxide in the brain is found

Department of Histology and Central Research Laboratory, Omsk Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 7, pp. 12-14, July, 1983. Original article submitted November 18, 1982.

 0007-4888/83/9607-0892$07.50

TABLE 1. Brain Tissue LPO Parameters during Ischemia and Postischemic Period (M ± m)

Time of investigation	Antioxidant activity	Diene conjugates	MDA
	meq/g wet weight of tissue		
Ischemia	0,285±0,047	38,6±1,41	0,624±0,040
P	<0,05	<0,01	<0,001
Postischemic period			
30 min	0,278±0,059	40,3±2,80	0,832±0,155
P	<0,05	<0,05	<0,01
1 day	0,363±0,022	38,8±4,00	0,368±0,027
P	0,06	>0,05	>0,05
Control	0,422±0,021	31,5±0,93	0,406±0,021

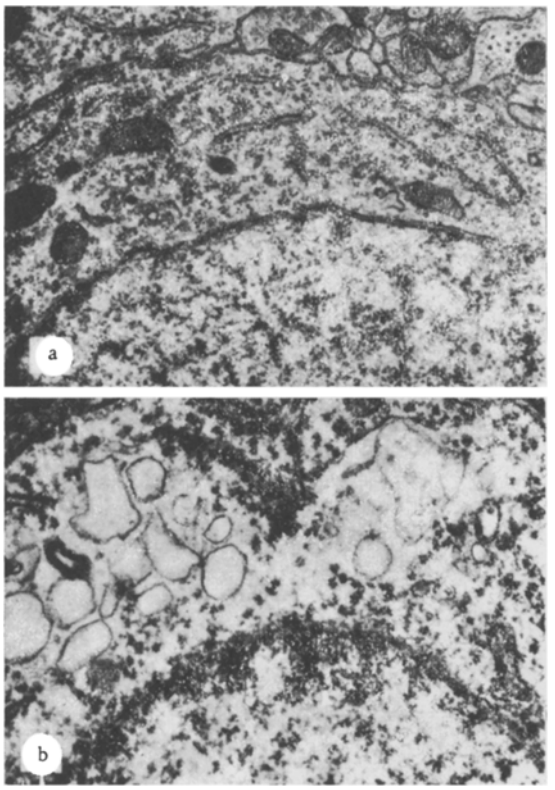

Fig. 1. Lysis and vacuolation of rough endoplasmic reticulum in cytoplasm of neuron in postischematic period: a) control, 12,000×; b) after 24 h, 14,000×.

6.5 min after mechanical asphyxia [2]. The harmful action of free radicals on membranous structures of nerve cells at the end of ischemia is demonstrated by the sharply increased concentration of diene conjugates and MDA in the brain. The mildness and limited spread of changes in neuron organelle ultrastructure at this time point to the development of fine injuries to the membranes at the molecular level. Lipid peroxidation in the brain in the early postischemic period is facilitated by the hypercatecholaminemia, lactacidosis, hyperoxygenation of the nerve tissue, and low activity of enzymes of antiradical and antiperoxide defense [2, 4]. The intensity of the ultrastructural disturbances of the neuronal organelles increases under these circumstances.

The small increase in antioxidant activity of brain tissue and the decrease in MDA concentration 24 h after ischemia reflect activation of compensatory mechanisms of defense of the lipid component of the membranes.

However, marked generalized lesions of neuronal membrane formations are evidence of progressive destructive processes in the cells. Profound disturbance of membrane ultrastructure mainly in neurons in the late stages of exposure to hypoxia has been reported in several publications [1, 6]. At this time the harmful action of other factors, and, in particular, of a broad spectrum of lysosomal enzymes, is manifested [3]. Excessive activation of LPO in the neurons during ischemia and in the early stages of recirculation evidently plays a leading role in the increased lysosomal membrane permeability and in the solubilization and decompartmentalization of acid hydrolases, and through peroxidation of membrane structures it creates optimal conditions for realization of the hydrolytic effect of the lysosomal enzymes.

The sharply intensified processes of LPO in brain tissue during ischemia and in the early postischemic period thus cause damage to membrane structures at the molecular level and lysosome formation, which aggravates subsequent destruction of the nerve cells.

LITERATURE CITED

1. N. N. Bogolepov, Ultrastructures of the Brain in Hypoxia [in Russian], Moscow (1979).
2. V. D. Konvai, Patol. Fiziol., No. 5, 30 (1982).
3. V. G. Korpachev and V. V. Semchenko, Patol. Fiziol., No. 6, 62 (1980).
4. V. A. Negovskii, A. M. Gurvich, and E. S. Zolotokrylina, Postresuscitation Sickness [in Russian], Moscow (1979).
5. I. D. Stal'maya and T. G. Garishvili, in: Modern Methods in Biochemistry [in Russian], Moscow (1977), pp. 66-68.
6. V. P. Tumanov and M. D. Malamud, Changes in the Central Nervous System after Thermal, Radiation, and Combined Trauma [in Russian], Kishinev (1977).
7. N. M. Émanuél', Vest. Akad. Nauk SSSR, No. 9, 66 (1981).
8. J. Fridowich, Adv. Neurol., 26, 255 (1979).
9. J. Glaving, Acta Chem. Scand., 17, 1635 (1963).
10. L. Placer, Nahrung, 12, 679 (1968).

CHANGES IN ORBITOFRONTAL AND SOMATOSENSORY CORTICAL ELECTRICAL ACTIVITY DURING ELECTROACUPUNCTURE

V. K. Reshetnyak, M. L. Kukushkin, and R. A. Durinyan

UDC 615.844.4.015.4:612.825.2.014.423

KEY WORDS: electroacupuncture; morphine; evoked potential; cortex.

Considerable attention has been paid to the study of the mechanisms of pain [2, 8, 9, 12, 13]. At the same time, the mechanisms of formation of reflex analgesia are being studied, as one of the most promising methods of treatment of acute and chronic pain syndromes [4, 5]. The present writers have shown [11] that electroacupuncture (EAP) considerably depresses the conduction of nociceptive impulses at the level of the primary relay nuclei without affecting transmission of nonnociceptive tactile afferent impulses. It has been shown that EAP blocks nociceptive impulses in the specific and nonspecific thalamic nuclei. In particular, depression of nociceptive impulses is stronger in the parafascicular complex than in the specific projection nuclei, in the ventromedial nucleus for example [10]. An essential role in the mechanisms of pain perception is played by the orbitofrontal and second somatosensory (SII) areas of the cortex [2, 4].

Central Research Institute of Reflex Therapy, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 7, pp. 14-16, July, 1983. Original article submitted June 4, 1982.

0007-4888/83/9607-0894$07.50