BIOPHYSICS AND BIOCHEMISTRY

Lipid Peroxidation Level in the Focus of Compression Ischemia in the Cerebral Cortex of Rats

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Pathomorphological changes in a focus of ischemia, the level of lipid peroxidation (as indicated by the content of products reacting with thiobarbituric acid), and the postischemic levels of adenyl nucleotides and tissue lipids were studied in rats with focal compression ischemia of the cerebral cortex. An increased level of the TBA-reactive products paralleled by a reduction of the concentrations of adenyl nucleotides and tissue lipids was found to be in clear-cut correlation with the processes of neuronal injury and death and with subsequent repair phenomena in the focus of cortical ischemia.

Key Words: *ischemia; brain; lipid peroxidation*

Cerebral ischemia is one of the most prevalent nervous and neurosurgical diseases. It may manifest itself as a separate disease (brain stroke) or as a complication of brain injury and various forms of brain compression (epi- and subdural hematomas, retraction ischemia in neurosurgical interventions). Among the principal mechanisms of ischemic diseases of the brain are the processes of free-radical formation and of lipid peroxidation (LPO) leading to injury of lipoprotein membranes and of neuronal cytoplasmic organelles, as well as to changes in the conformation of proteins, DNA, and, eventually, to the death of neurons [3,7]. The aim of this research was to measure the LPO level in the focus of ischemic infarct of the cerebral cortex of rats in various periods of its formation, development, and involution. The method of creating focal compression ischemia of the rat cerebral cortex [1], which may be regarded as an experimental model of retraction ischemia in clinical neurosurgery [4,6], was used in our study.

MATERIALS AND METHODS

Male Wistar rats weighing 200 to 250 g were used in the experiments. The head of the anesthetized animal was fixed in the head-clamp of a stereotaxic device. After a longitudinal incision of the skin the periosteum was separated and a hole 5 mm in diameter was drilled in the parietal bone with a cylindrical bore. The dura mater was dissected. A pressure on the cortical surface equal to 40 mm Hg was produced with a 3.5-mm rod. After 15 min the rod was removed and the wound sutured.

The material for pathomorphologic and biochemical studies was collected 2, 5, 16, and 24 h postoperation and on days 4 and 7. An area of the parietal cortex standard in volume and weighing about 40 mg, including the ischemic focus, was dissected and homogenized in 2 ml of 80% ethyl alcohol. Symmetrical areas of the contralateral pa-

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rietal cortex were examined for control. Denatured proteins were sedimented by centrifugation. Aliquots of alcohol extracts were treated with 0.5% 2-thiobarbituric acid (TBA) in the presence of 1% orthophosphoric acid. The concentration of TBA-reactive products was assessed spectrofluorometrically in butanol extracts by the routine method [2]. Besides TBA-reactive products, the concentrations of lipids and adenyl nucleotides (mainly ATP) were assessed spectrophotometrically by the specific absorption at 200 and 259 nm.

RESULTS

The ischemic focus encompassing the entire transverse section of the cortex was visualized by staining the slices of nonfixed brain with triphenyltetrazolium chloride [5] 24 h after compression of the brain surface. The focus of cortical necrosis and the marginal zone (penumbra) containing both degenerating and intact neurons were discernible in hematoxylin-eosin-stained histological slices as early as on day 2. Small hemorrhages were seen in the zone of infarction and in the underlying white matter. Later, at the end of the first week postoperation, a gliomesodermal cicatrix began to form in the zone of cortical infarction.

As is seen in Fig. 1, the level of LPO products in the ischemic focus increases approximately twofold during the first 24 h after compression of the cortex and remains elevated on day 4, a clear-cut tendency toward normalization of the TBA-reactive products in the damaged tissue not being observed until the 7th day. Interestingly enough, LPO intensification in the focus of compression ischemia is paralleled by a marked (almost twofold at 24 h) decrease of the adenyl nucleotide level. This may be indicative of suppressed energy metabolism in the ischemized portion of brain tissue. At the same time, the decrease in the level of tissue lipids is somewhat delayed and less pronounced, the amount being approximately 70% of the baseline level. This evidently reflects postischemic neuronal degeneration. Recovery of the tested biochemical parameters by day 7 correlates with the pathomorphological data and is a manifestation of repair processes in the injured nervous tissue.

In sham-operated animals (in which a cranial hole was drilled and the dura mater dissected, but

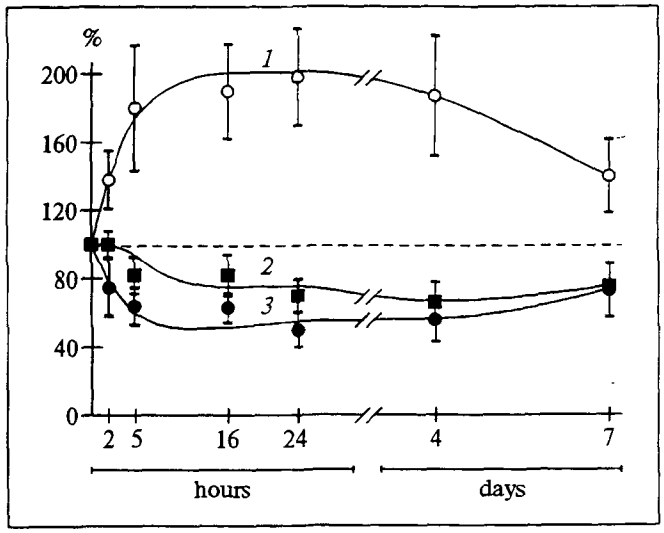

Fig. 1. Time course of TBA-reactive products (*1*) and of concentrations of tissue lipids (*2*) and adenyl nucleotides (*3*) in the postischemic period. Abscissa: time.

no compression of the brain was performed) neither the level of adenyl nucleotides, nor the lipid content in cerebral tissues changed, although a negligible (less than 20% 5 h postoperation) increase in the content of LPO products was observed. Moreover, sham operations as a rule were not attended by marked destructive changes in the cortical neurons. These results indicate that in local compression ischemia of the brain LPO activation may appreciably contribute to neuronal injury. Therefore, exploring the use of antioxidants for mitigating neuronal degeneration and for stimulating repair processes in retraction ischemia associated with neurosurgical interventions appears to be a promising trend of research.

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