Free Radical Lipid Oxidation in Brain Cortex Neurons and Neuroglia during Convulsions

M. A. Flerov, T. I. Tolstukhina, and I. A. Gerasimova

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The amount of lipid peroxidation products (conjugated dienes and trienes and Schiff bases) in cortical neurons of the cerebral hemispheres decreased by 30% at the peak of convulsions observed 10-15 min after intraperitoneal injection of picrotoxin. In neuroglial cells of control animals the intensity of lipid peroxidation in was 1.7-2.0 times lower. Picrotoxin had no effect on this parameter.

Key Words: *lipid peroxidation; neurons; neuroglia; convulsions*

Free radical lipid oxidation is a mechanism underlying changes in the composition and physicochemical properties of the membrane bilayer, which plays a role in various processes occurring in the central nervous system (CNS). Under physiological conditions lipid peroxidation (LPO) is involved in the maintenance of structural integrity and functional plasticity of membranes and provides activity of ion channels, receptors, and enzymes [1,8].

Profound changes in the intensity of LPO have serious functional consequences and contribute to the development of diseases. The study of radical generation in CNS during convulsion [2,7] accompanying nervous and mental disorders is of considerable importance [4]. Much attention was paid to the molecular pathogenetic mechanisms of convulsive activity. Little is known about lipid metabolism (*e.g.*, free radical lipid oxidation) in various cells, including neurons and neuroglia [2,4,7]. These cells have various metabolic functions and play different roles in hyperactivation of the nervous system. Here we studied the intensity of free radical lipid oxidation in neuronal and glial fractions of the brain cortex under normal conditions and during convulsions induced by picrotoxin.

MATERIALS AND METHODS

Experiments were performed on male outbred albino rats weighing 120-150 g. Convulsions were induced by intraperitoneal injection of 0.25% picrotoxin in a dose of 0.2 ml per 100 g body weight. The rats were decapitated at the peak of convulsive activity, *i.e.* 10-15 min after administration of the convulsant. The brain was rapidly removed and washed from the blood with cold physiological saline. The brain cortex was isolated and thoroughly minced on cold glass plates. Cell fractions enriched with neurons and neuroglia were isolated [11]. Lipid extraction and quantitative study of phospholipids, conjugated dienes (CD), conjugated trienes (CT), and Schiff bases (SB) were performed as described elsewhere [12]. The content of LPO products was expressed in arb. units per 1 mg phospholipids. The results were processed using Student's *t* test.

RESULTS

In control animals the intensity of LPO in cortical neurons was much higher than in the neuroglia (Table 1). The content of CD, CT, and SB in neurons surpassed that in the neuroglia by 3, 2, and 1.7 times, respectively. These data suggest that neuronal cells with low content of phospholipids contains considerable amounts of LPO products [10]. Probably, neuronal phospholipids characterized by higher content of polyunsaturated fatty acids more easily undergo free radical oxidation compared to the neuroglia [14]. Specific features of the antioxidant system in various cell populations should be taken into account. Glial cells

Laboratory of Neuroendocrinology, I. P. Pavlov Institute of Physiology, Russian Academy of Sciences, St. Petersburg

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are more resistant to free radical oxidation [6], intensively degrade hydroperoxides, and are characterized by higher activity of antioxidant enzymes [15]. It should be emphasized that the system of antioxidant protection in neurons is mainly presented by antioxidant compounds, including α-tocopherol [3,15]. Taking into account these differences in the prooxidant/antioxidant state, it can be hypothesized that the intensity of lipid oxidation in neurons and neuroglia would undergo various changes during convulsions.

At the peak of convulsive activity the amount of LPO products decreased more than by 30% in neuronal cells, but remained practically unchanged in the neuroglia (Table 1).

At first glance it would seem that our results contradict published data on the role of LPO in convulsive activity [2]. The development of convulsions is associated with a sharp increase in the intensity of peroxidation. Previous studies demonstrated that radical products act as physiological messengers of convulsive disorders [9]. Therefore, antioxidants are extensively used in the treatment of these disturbances. However, it is clear that external factors produce phasic changes in the intensity of free radical processes. The type, degree, and dynamics of the response depend on the strength, duration, and nature of stimulation [5]. The system of prooxidants and antioxidants differs in neurons and neuroglia. These data suggest that neurons and neuroglia would exhibit different reactions to external stimulation. The antioxidant system in neurons is probably activated 10-15 min after picrotoxin administration. Under these conditions the inhibition of free radical oxidation precedes its activation during convulsions. The inhibition of LPO determines high plasticity of neuronal membranes and provides conditions for hyperactivation of neurons during convulsions. Long-term hyperactivation of neurons is followed by exhaustion of the antioxidant system and strong activation of radical generation. Probably, antioxidant enzymes of neuroglial cells are involved at later stages and are responsible for long-term adaptation of neurons to hyperactivation.

Our previous studies showed that metabolism of lysophosphatidylcholine and phosphatidic acid in neurons increases during convulsions, which reflects activation of phospholipase hydrolysis in these cells [13]. Activation of phospholipases is associated with LPO and protects the cell membrane from peroxidation.

TABLE 1. Content of LPO Products in Brain Cortex Neurons and Neuroglia of Rats under Physiological Conditions and during Convulsions (arb. U/mg phospholipids, $M \pm m$, $n=6$)

LPO products		Neurons	Neuroglia
CD	control	1.34±0.08	0.44±0.03
	picrotoxin	0.97±0.09*	0.50±0.03
CT	control	0.63±0.06	0.28±0.02
	picrotoxin	0.44±0.05*	0.33±0.02
SB	control	292±5	173±21
	picrotoxin	184±18*	195±10

Note. *$p<0.05$ compared to the control.

Unsaturated fatty acids formed during hydrolysis of phospholipids can serve as a free radical trap. It can be hypothesized that inhibition of LPO in neurons during convulsions is at least partly related to phospholipase activation.

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