QUALITATIVE AND QUANTITATIVE CHANGES IN THE BRAIN PHOSPHOLIPID SPECTRUM OF RATS WITH METRAZOL SEIZURES

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Seizure activity is characterized by disorders of function of membrane-bound enzymes [5, 7, 6, 9], a decrease in the number of receptors [10], and an increase in the transbilayer "flip-flop" transport of phospholipids (PL) under the influence of neurotransmitters [6] and by the probable hydrolysis of phosphatidylinositols (PI), which are involved in the transmission of nervous impulses and play the role of suppliers of PI and diglyceride as secondary messengers [3, 4, 11], responsible for maintaining functional activity of the cell.

In view of the facts described above and considering the role of lipids in the structural and functional organization of biological membranes [2], we set out to undertake a special study of the changes in PL—PL relations in the cerebral and cerebellar cortex of normal rats and rats with metrazol seizures.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats weighing 150-200 g, kept on an ordinary diet. Generalized epilepsy was induced by intraperitoneal injection of metrazol in a dose of 45 mg/kg body weight.

Under visual observation (time and motion study) the latent period of appearance of seizures lasting 6-10 min was noted and the number of clonicotonic seizures was counted and their intensity determined. Brain samples for determination of qualitative and quantitative composition of PL were taken from animals killed at the peak of epileptic activity. Individual PL were fractionated by unidimensional ascending chromatography in a thin layer of silica-gel ("Chemapol," Czechoslovakia), using a system of solvents of chloroform—methanol—ammonia (65:35:5). The spots of PL fractions were identified with the aid of reference substances, and the lipid phosphorus was mineralized in a medium of sulfuric and nitric acids and expressed quantitatively in μg/mg dry tissue [1].

EXPERIMENTAL RESULTS

The experiments showed that during seizures there was a definite and statistically significant increase in the total PL in the cerebral cortex followed by a decrease until 1 h after the epileptic fit, although it remained rather higher than the control level.

Despite the high level, the initial PL content in the cerebeltam was statistically significantly lower than in the cerebral cortex both during the seizure and for 1 h thereafter.

The effect of mutual transformations of PL-glycerides during seizures, with an increase in the content of phosphatidylserines (PS) and lysophosphatidylcholines (LPC) in both cerebral and cerebeltar cortex is given in Table 1. Meanwhile a decrease in the phosphatidylcholine and phosphatidylethanolamine (PE) concentrations was observed. In the cerebellum, under the influence of the epileptogen, there was a decrease in concentrations of cardiolipins-1 and a mixed fraction consisting of sphingomyelin and PI, with an increase in the cardiolipin-2 concentration.

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TABLE 1. Composition of PL (in % of total lipid P) in Cerebral and Cerebellar Cortex of Albino Rats under Normal Conditions and during Epileptic Fit (M ± m)

Experimental conditions	LPC	PS	Sphingomyelin, phosphatidylinositol	Phosphatidylcholine	PE	Cardiolipin-1	Cardiolipin-2
Cerebral cortex							
control	2.85±0,17	3,63±0,21	15,34±0,36	37,04±0,32	33,57±0,24	3,76±0,19	3,82±0,20
seisure	4,03±0,24**	4,56±0,33*	16,49±0,42*	34,25±0,51***	32,51±0,37*	4,33±0,14*	3,82±0,18
Cerebellum							
control	3,64±0,35	4,81±0,15	18,68±0,39	38,45±0,49	25,24±0,38	5,25±0,36	3,94±0,22
seizure	5,93±0,50**	5,71±0,19**	17,93±0,27*	36,68±0,54*	23,54±0,27**	4,93±0,28*	5,28±0,27**

Legend. *p < 0.02, **p < 0.002, ***p < 0.001.

The changes observed in the various PL fractions, together with the relatively stable background of the total of these compounds confirm the existing view [14] of the great physiological importance of constancy of the qualitative and quantitative relations between the substances mentioned. We are inclined to explain the increase in the PS concentration against the background of metrazol seizures by the role of PS-decarboxylase [14], which catalyzes the reversible reaction of interconversions of PS and PE. It is not difficult to understand that conversions of phosphatidylcholine against the background of metrazol seizures proceed along the lines both of their conversion into PS and of the formation of LPC. It will be clear that the increased yield of LPC is accompanied by an increase of the pool of nonesterified fatty acids [12], with the formation of considerable concentrations of lipid peroxides from them, substances characterized by a toxic, destructive, and inactivating action, especially on membrane receptors [6, 7].

The qualitative and quantitative shifts in the PL composition at different periods of seizure activity mentioned above can be correlated with changes in brain levels of certain mediators. According to data in the literature, during the onset and development of seizures, the most marked changes take place in the GABA-ergic systems of the brain. For instance, we know that in metrazol seizures there is a sharp decrease in the GABA level in the brain. Further support is given by the fact that combined administration of GABA and PS leads to termination of the seizures [15], i.e., it can be postulated that PS may have a potentiating effect on the inhibitory action of GABA. The possibility likewise cannot be ruled out that the noradrenergic system of the brain participates in the mechanisms of these changes, for previous investigations [13] have demonstrated its characteristic property of exerting a definite inhibitory action on the formation of seizure activity.

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