Effects of S-Adenosyl Methionine, Ethanolamine, and Their Combination on Lipid Composition of Rat Brain in Chronic Alcohol Intoxication

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Brain lipids are studied in rats with chronic alcohol intoxication after injection of S-adenosyl methionine, ethanolamine, and their combination. The levels of total lipids, phospholipids, and cardiolipin are increased and those of sphyngomyelin and cerebrosides-III decreased after a 14-day inhalation of ethanol. Combined administration of S-adenosyl methionine and ethanolamine in chronic alcoholization eliminated ethanol-induced shifts in concentrations of phospho- and glycolipid fractions in rat brain.

Key Words: *brain; alcohol; phospholipids; glycolipids*

Alcohol neurotoxicity is a fact universally acknowledged [7,13]. Disorders in lipid metabolism and shifts in lipid structure of nerve tissue membranes play an important role in the mechanisms of alcohol dependence and toxic effect of ethanol [10]. The search for effective measures protecting from untoward effect of alcohol does not rule out the use of agents stabilizing lipid composition. Ethanolamine (EA) deserves special attention as a component of phospholipids and a compound structurally similar to ethanol. As a natural metabolite with very low toxicity, EA decreases the manifestation of alcohol intoxication in rats [8] and the duration of narcotic sleep caused by alcohol [1]. S-adenosyl methionine (SAM) participates in phosphatidyl ethanolamine transmethylation during phosphatidyl choline biosynthesis. Methylation processes in the brain are believed to contribute to the development of convulsions [11] in many neurological diseases, including chronic alcoholization and the abstinence syndrome.

We compared the effects of SAM, EA, and their combination on the levels of some lipids in the brain of rats exposed to chronic alcohol intoxication (CAI).

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MATERIALS AND METHODS

Male rats weighing 160-180 g kept under standard conditions were used, 8 animals per group. CAI was induced by 14-day inhalations of ethyl alcohol vapor in a 0.6 m^3 chamber at ethanol concentration of about 30 mg/liter. Controls were exposed to humidified air in a similar chamber. The abstinence syndrome was assessed 10 h after the rats had been removed from the chamber as described previously [5]. SAM (50 mg/kg) was injected intraperitoneally three times every 3 h after ethanol withdrawal, EA (100 mg/kg) intraperitoneally 1 h before decapitation. In combination, the drugs were used in the same doses.

Lipids were extracted and purified by modified Folch's method [6,3]. The levels of total lipids, cholesterol, phospholipids, and triglycerides were measured as described previously [3]. Phospholipid fractions were separated in a thin layer of silica gel in a chloroform:methanol:water system (65:25:4), glycolipid fractions in chloroform:methanol:concentrated ammonium solution (80:20:0.4) [3]. Phospho- and glycolipids were estimated by the phosphorus and carbohydrate component, respectively [4,12]. The data were processed by variation statistics analysis using Student's test.

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Table 1. Effect of SAM, EA, and SAM+EA on Brain Content of Total Lipids, Cholesterol, Triglycerides, Phospholipids (mg/g tissue), and Their Fractions (%) in Rats after Chronic Inhalation of Ethanol (*M±m*, *n*=8)

Parameter	Control	Ethanol	Ethanol+SAM	Ethanol+EA	Ethanol+SAM+EA
Total lipids	105.6±1.4	118.5±3.1*	113.3±1.3*	113.1±2.7*	109.5±2.6
Cholesterol	16.9±0.9	15.8±1.1	16.7±0.4	17.8±1.1	18.8±0.6
Total phospholipids	39.7±0.8	41.7±0.6*	40.7±0.4	41.6±0.5*	40.9±0.5
Triglycerides	7.8±0.4	7.5±0.5	7.5±0.4	8.3±0.5	7.9±0.6
Sphyngomyelin	14.5±0.7	11.8±0.5*	11.9±0.4*	13.6±0.8*	13.2±0.9
Phosphatidylcholine	42.9±1.9	43.1±1.1	45.0±1.2	44.5±1.5	41.4±1.5
Phosphatidylethanolamine	31.6±1.3	33.1±0.8	33.3±0.7	32.2±1.3	32.6±1.7
Cardiolipin	8.6±0.7	11.1±0.9*	10.0±1.1	11.8±0.8*	11.0±1.2

Note. Here and in Table 2: *changes are significant in comparison with control group, *in comparison with the group exposed to ethanol.

Table 2. Effect of SAM, EA, and SAM+EA on Brain Glycolipid Fractions (mg/g Tissue) in Rats after Chronic Ethanol Inhalations (*M±m*, *n*=8)

Parameter	Control	Ethanol	Ethanol+SAM	Ethanol+EA	Ethanol+SAM+EA
Sulfatides-I	3.74±0.17	3.42±0.25	3.48±0.17	4.33±0.18**	3.77±0.22
Sulfatides-II	2.55±0.19	2.27±0.22	2.97±0.18	4.11±0.31**	2.98±0.21
Cerebrosides-I	3.03±0.25	2.57±0.23	2.94±0.18	3.22±0.24	3.10±0.20
Cerebrosides-II	2.54±0.12	2.25±0.11	2.58±0.17	2.41±0.17	2.65±0.24
Cerebrosides-III	4.14±0.17	2.70±0.23*	3.69±0.30*	3.71±0.39*	3.57±0.23*

RESULTS

Tonic clonic convulsive paroxysms typical of physical dependence were observed in 86% rats exposed to inhalation of ethanol after its discontinuation. After SAM injection, the abstinence syndrome was observed only in 28.5% animals. No signs of convulsive activity were observed in rats injected EA alone or in combination with SAM.

The concentrations of total lipids, phospholipids, and cardiolipin increased, while those of sphyngomyelin (Table 1) and cerebrosides-III (Table 2) decreased in the brain of rats exposed to 14-day ethanol inhalation. These results agree with the data of others [2,9].

SAM alone eliminated the differences from the control in the content of total phospholipids and cardiolipin (Table 1); the level of cerebrosides-III increased (Table 2).

EA virtually did not protect the majority of the studied lipids in the brain, except sphyngomyelin and cerebrosides-III, whose contents were normalized. The content of sulfatides-I and -II in nerve tissue increased in comparison with the control (Table 2).

It is noteworthy that combined use of SAM and EA in CAI eliminated shifts in brain contents of phospho- and glycolipids caused by ethanol. Therefore, a combination of SAM and EA is recommended for arresting the abstinence syndrome and correcting lipid disorders in the brain in CAI.

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