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EFFECT OF N-STEAROYLETHANOLAMINE ON THE LIPID COMPOSITION OF THE FRONTAL CORTEX AND HIPPOCAMPUS OF THE RAT'S BRAIN AT THE AGING

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Brain aging is an integral part of biological aging and is one of the most pressing medical and social issues today [1]. Lipids act as important regulators of various biological processes, including aging of the brain. Lipids play an important role in ensuring the structure of the brain and the regulation of its work. With age, the human brain decreases in most classes of lipids and fatty acid composition of brain tissues [2, 3].

Aim. It is important to study the possible protective effect of cannabimimetic lipid — N-stearoylethanolamine (NSE) on the lipid composition of the frontal cortex, hippocampus and on the state of episodic memory of old rats.

Methods. Experimental models on animals: the white outbred male 18-month-old rats (n=20) were used to investigate the influence of NSE treatment on the lipid composition of brain structures and young animals served as a control group. The water suspension of NSE at a dose 50 mg/kg was administered to old rats.

Extraction of lipids from the tissues of the hippocampus and frontal cortex of rats was performed by the method of Bligh and Dyer. Phospholipids were separated by two-dimensional thin layer chromatography. Methyl esters of fatty acids from lipid extract were obtained by a modified method of Carreau and Dubaco. Quantitative analysis of fatty acid methyl esters was performed by gas-liquid chromatography on an Agilent GC7890 chromatograph with an Agilent 8987 mass detector. The fractions of free and esterified cholesterol were separated by one-dimensional thin layer chromatography. The dry cholesterol residue was analyzed on a Carlo Erba gas-liquid chromatograph. Behavior test "New object recognition" Animal testing was performed twice — the first test was performed before the animals were divided into experimental groups, the second test was performed after the introduction of NSE. Statistical analysis was performed using Student's t-test, data at $P < 0.05$ were considered reliable.

Results. The study of the diacyl (DF) and plasmalogen (PF) forms of phospholipids (PLs) content in the frontal cortex and hippocampus have shown a significant decrease in the plasmalogen form of PE (Phosphatidylethanolamine) (up to 15%) and an increase in its DF, compare to its content in young rats. Administration of NSE to old rats led to a significant increase in PF PE and didn't cause significant changes in the content of PF in the composition of other PL of the frontal cortex of the brain and hippocampus (Table). The decrease in the percentage of various phospholipids was found in frontal cortex and hippocampus of old rats: the content of phosphatidylcholine (PC) and phosphatidylinositol (PI) was significantly reduced in the frontal cortex and the decrease of diphosphatidylglycerol (DPG), PI and phosphatidylserine (PS) was found in the hippocampus, compare to the young animals.

Administration of NSE to old rats had a different effects on the content of various phospholipids. The increase in the content of PC and PI in the frontal cortex and PS and DPG in the hippocampus is particularly pronounced due to NSE. It is known that DPG is a necessary PL for the functioning of the electron transport chain of mitochondria, and, consequently, to maintain cell energy (Table).

An increase in the content of saturated fatty acids (FFAs) and a decrease in the content of unsaturated FFAs in the frontal cortex and hippocampus of old rats also has been found. In particular, significantly reduced the content of polyenoic and monoenoic FFAs. The NSE administrations led to reducing the content of saturated FFA, normalizing the content of unsaturated FFA by increasing mono- and polyenoic FFA.

It has also been found that NSE administration to old rats promoted the growth of the free cholesterol level in the frontal cortex and hippocampus (Table).

Table. Effect of N-stearoylethanolamine on the lipid composition of the frontal cortex and hippocampus of the rat's brain at the aging, and discrimination rate of the "New object recognition" test at the aging

Indicators	Control group	Old rats	Old rats + NSE
Frontal cortex			
PC DF (%)	70 ± 1.13	94.45 ± 1.51 *	93.48 ± 1.24 #
PC PF (%)	30 ± 1.13	5.55 ± 1.51*	6.52 ± 1.24 #
PE DF (%)	39.55 ± 1.38	88.20 ± 1.84 *	56.01 ± 5.22 #
PE PF(%)	60.45 ± 1.38	11.80 ± 1.84 *	43.99 ± 5.22 #
PC (%)	34.64 ± 0.38	31.59 ± 1.35 *	36.26 ± 0.81 #
PI (%)	7.5 ± 0.36	3.87 ± 0.16 *	7.27 ± 0.44 #
Cholesterol (μg/g lipids)	5000 ± 500	3500 ± 350 *	4500 ± 580 #
Hippocampus			
PC DF (%)	71.94 ± 0.92	95.93 ± 1.23 *	92.35 ± 0.16 #
PC PF (%)	3.06 ± 0.92	4.07 ± 1.23 *	7.65 ± 0.16 #
PE DF (%)	35 ± 1.51	57.24 ± 2.01 *	49.35 ± 2.80 #
PE PF (%)	65 ± 1.51	42.76 ± 2.01 *	52.89 ± 2.89 #
DPG (%)	3.46 ± 0.26	2.65 ± 0.01 *	3.84 ± 0.46 #
PI (%)	9.21 ± 0.6	6.58 ± 0.03 *	6.9 ± 0.89 #
PS (%)	15.67 ± 0.32	10.14 ± 0.58 *	12.39 ± 0.25 *#
Cholesterol (μg/g lipids)	3000 ± 500	2500 ± 350 *	2600 ± 580 #
Discrimination index of the "New Object Recognition" test	0.376667 ± 0.02	0.20598 ± 0.035 *	0.296624 ± 0.03 #

Notes: PF — plasmalogen form, DF — diacyl form, PC — phosphatidylcholine, PE – phosphatidylethanolamine, PI — phosphatidylinositol, PS — phosphatidylserine, DPG — diphosphatidylglycerol, % — of the total amount of phospholipids, * — $P < 0.05$ compared to the group "Control group", # — $P < 0.05$ compared to the group "Old Rats".

The results of the New Object Recognition test in old rats have shown that a short-term memory has been improved by NSE (Table).

Conclusions. The administration of NSE to old rats causes an increase in PF of PLs in the frontal cortex and hippocampus of the brain, which can be considered as one of the mechanisms of neuroprotective action of NSE in aging. The changes in the phospholipids and fatty acids composition, and free cholesterol level of the frontal cortex and hippocampus of the brain of old rats caused by NSE administration have been shown to be adaptive and restorative. The New Object Recognition Behavioral Test has shown that NSE restores short-term memory in older rats.

The obtained results expand the understanding of the mechanisms of biological action of NSE during aging in mammals and create the basis for the development a new drug with geroprotective properties.

Key words: N-stearoylethanolamine, aging, phospholipids, plasmalogens, fatty acids, cholesterol, memory.

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