Effects of Potentiated Antibodies Against Brain-Specific S100 Protein on Biogenic Amine Content and Lipid Peroxidation in Rats under Conditions of Alcoholization

A. M. Titkova, I. R. Pan, and O. I. Epstein*

Antibodies against S100 protein in ultralow doses specifically affected catecholamine metabolism in rats withdrawn from chronic ethanol exposure. The contents of tryptophan, tyrosine, and norepinephrine in brain structures returned to normal. The concentrations of dopamine, epinephrine, and norepinephrine in the peripheral blood decreased. Modulation of monoamine content in the peripheral blood suggests that antibodies against S100 protein possess stress-protective activity during ethanol withdrawal.

Key Words: *ultralow doses; antibodies against S100 protein; ethanol; biogenic amines; lipid peroxidation*

We studied the effects of potentiated antibodies against S100 protein in ultralow doses (PAB-S100) on central monoaminergic and peripheral hormonal-and-metabolic effects of chronic ethanol exposure in rats.

MATERIALS AND METHODS

Experiments were performed on male outbred rats weighing 200-250 g. The animals perorally received 25% ethanol in a dose of 1.5-2.0 g/kg for 15 days. After ethanol withdrawal some animals were treated with 0.1 ml PAB-S100 (dilution C1000, equivalent concentration 10^{-2000} wt %) 2 times a day for 7 days. The rats were decapitated on the next day after the last treatment. The contents of biogenic amines (dopamine, norepinephrine, epinephrine, and serotonin) and their amino acid precursors (tyrosine and tryptophan) were measured in the hypothalamus, frontal neocortex, and whole blood. Blood histamine level was estimated [6]. The concentrations of malonic dialdehyde (MDA) [3] and conjugated dienes [1] and acetylcholinesterase (AChE) activity [5] were determined in blood plasma.

The results were analyzed by Statgraphics software.

Institute of Neurology, Psychiatry, and Narcology, Ukrainian Academy of Medical Sciences, Kharkov; *"Materia Medica Holding" Research-and-Production Company, Moscow

RESULTS

No significant changes were revealed in the frontal cortex and amygdaloid complex 7 days after ethanol withdrawal. The contents of tryptophan and serotonin in the hypothalamus and hippocampus remained unchanged. However, catecholamine content in these structures underwent opposite changes. The concentrations of norepinephrine and epinephrine in the hypothalamus decreased by 45 and 29%, respectively. In the hippocampus the contents of dopamine, norepinephrine, and epinephrine increased by 2.5-4 times. These changes were probably associated with motivational excitation of animals [4].

PAB-S100 prevented these changes. Norepinephrine content in the hypothalamus increased, but catecholamine level in the hippocampus decreased. In rats receiving PAB-S100 tryptophan content in the hippocampus and amygdaloid complex and serotonin concentration in the amygdaloid complex decreased compared to those in alcoholized animals. These changes may attenuate the inhibitory effect of serotonin in the amygdaloid complex [2].

The metabolism of neuromediators in the peripheral blood from alcoholized rats remained practically unchanged. We revealed an increase in the concentration of lipid peroxidation products (particularly conjugated dienes, up to 191%), which probably reflects inactivation of endogenous antioxidant systems. PAB-

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TABLE 1. Contents of Biogenic Amines (nmol/liter) and Amino Acid Precursors (mmol/liter) in Rat Brain Structures ($\bar{X}\pm m$, n=7-11)

Brain structure, parameter	Intact	Ethanol	Ethanol and PAB-S100
Frontal cortex			
tyrosine	7.1±0.6	5.80±0.36	5.62±0.51
dopamine	2.40±0.17	2.67±0.50	2.79±0.23
norepinephrine	1.90±0.18	1.50±0.31	1.62±0.31
epinephrine	0.54±0.07	0.35±0.06*	0.34±0.03*
tryptophan	13.0±1.4	5.68±1.22*	10.07±1.31
serotonin	3.00±0.34	3.32±0.23	2.40±0.42
Hypothalamus			
tyrosine	19.5±2.3	29.10±3.55**	20.31±1.36*
dopamine	4.70±0.58	4.51±0.54	4.20±0.38^{+}
norepinephrine	3.90±0.41	2.22±0.39*	4.81±0.89**
epinephrine	1.06±0.12	0.75±0.07*	0.59±0.10
tryptophan	19.8±1.9	20.48±4.23	20.22±3.36
serotonin	8.10±0.94	9.08±1.27	8.81±0.85
Amygdaloid complex			
tyrosine	10.2±0.7	13.58±1.34	9.07±0.60
dopamine	3.90±0.28	4.39±0.40	4.03±0.31
norepinephrine	1.40±0.16	1.52±0.24	1.74±0.18
epinephrine	0.49±0.05	0.55±0.07	0.42±0.07
tryptophan	18.3±2.1	25.05±4.11	15.81±1.79
serotonin	5.00±0.54	5.26±0.32	6.61±0.86
Hippocampus			
tyrosine	9.1±1.6	12.41±1.86	15.15±1.18*
dopamine	1.80±0.19	4.95±0.77*	2.61±0.22
norepinephrine	1.90±0.23	8.48±1.87*	2.58±0.45^{+}
epinephrine	0.35±0.05	1.17±0.22*	0.53±0.07^{+}
tryptophan	5.70±0.31	5.52±0.66	4.47±0.44^{*+}
serotonin	3.20±0.38	3.28±0.53	4.49±0.58

Note. Here and in Table 2: *p<0.05 and **p<0.01 compared to intact rats; ^{+}p<0.05 and ^{++}p<0.01 compared to ethanol-receiving animals.

TABLE 2. Contents of Biogenic Amines (nmol/liter) and Amino Acid Precursors (mmol/liter) in the Whole Blood and AChE Activity (nmol/mg protein/min) and Concentration of Lipid Peroxidation Products (mmol/liter) in Blood Plasma from Rats ($\bar{X}\pm m$, n=7-11)

Material, parameter	Intact	Ethanol	Ethanol and PAB-S100
Blood			
tyrosine	10.7±1.0	10.30±1.45	11.44±0.83
dopamine	80.6±6.5	64.43±7.20	51.14±2.65*
norepinephrine	69.3±5.7	53.43±5.86	41.14±3.51*
epinephrine	37.1±3.3	45.29±5.41	20.14±1.84^{*++}
tryptophan	16.2±0.9	21.21±2.74	23.87±2.29
serotonin	807±50	885.14±87.18	1104.14±63.48
histamine	1685±91	1570.71±82.42*	1606.57±69.79
Plasma			
AChE	2.50±0.22	2.61±0.16	2.30±0.16
MDA	11.8±0.6	16.38±3.13	15.09±2.10
conjugated dienes	50.9±9.9	97.02±11.03^{+}	81.91±6.78

S100 slightly decreased the content of lipid peroxidation products (161%, statistically insignificant). PAB-S100 decreased catecholamine level and increased tryptophan concentration in the blood. These changes indicate that the preparation possesses anxiolytic properties [7].

Our results show that PAB-S100 specifically modulate catecholamine metabolism. The preparation prevented changes in brain structures and produced the peripheral inhibitory effect in alcoholized rats. These findings indicate that PAB-S100 hold much promise for the therapy of patients with the withdrawal syndrome.

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