Effects of Lead Administered to Pregnant Rats on the Brain of Their Offspring (Delayed Consequences)

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Low neuronal density in the neocortex, low serotonin concentration in the brain stem and hemisphere, 2-fold reduced norepinephrine content in the brain stem, and behavioral disorders were found in 40-day-old offspring of female rats treated with lead on day 18 of pregnancy.

Key Words: *brain; offspring; lead*

Lead affects functional state of the nervous system [1,2,11], especially in children (high lead concentration in bones is associated with asocial, aggressive, or even criminal behavior) [2,11]. The intelligence quotient correlates with dentinal lead content in schoolchildren. Lead crosses the placental barrier and is found in breast milk [11]. Therefore, studies of delayed lead effects on developing brain are of prime interest.

MATERIALS AND METHODS

The offspring (n=19) of 3 rat dams receiving 200 mg/kg $PbNO_3$ (4% water solution through a gastric tube) on day 18 of pregnancy was examined. The offspring (n=36) of 4 intact rats served as the control. Dams and their offspring were kept in the same vivarium with *ad libitum* food and water supply. Total exploratory activity of 1-month-old animals was studied in an elevated plus-maze (EPM) [11]. The rats were placed to the center of EPM (5 min). Total locomotor activity was estimated by the time spent in open arms, number of hang down movements, total time spent in open and closed arms, and the number of arm entries. The active exploratory, displacement, and passive exploratory behavioral profiles were evaluated by the number of rearings, grooming reactions, and sniffins, respectively. Each parameter was expressed in percents of the control. Rats aging 40 days were decapitated, and the body weight and weight of the brain were measured. Paraffin sections (7 μ width) from the left anterioparietal and parietal lobes stained with 1% methylene blue were examined, the width of the cortex and its molecular layer were determined, and the mean number of neurons in a standard vision field in layers I and V were calculated. In the right hemisphere the contents of epinephrine, norepinephrine, dopamine [4,9], histamine, and serotonin [12] were measured on a spectrofluorometer (Hitachi).

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RESULTS

Prenatally treated rats had greater body weights compared to control animals, which was probably due to their lower number in litters (6-8 *vs*. 8-12 in the control, Table 1). The absolute weight of the brain and width of the cortex and its molecular layer in treated and control rats were similar, while the relative weight of the brain in treated rats was 18.4% lower than in the control. Neuronal densities in the cortical layer V of the anterioparietal and parietal lobes in treated rats were lower than in the control by 14 ($0.05<p<0.1$) and 41% ($p<0.05$), respectively. Destructive lesions in the

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neocortex and hippocampus (necrotized neurons, proliferating neuroglial cells, and lymphoid elements) were found in some rats (Fig. 1).

The total time of motion in EPM for treated rats (a parameter reflecting the total locomotor activity) surpassed the control level by 19%. The number of active exploratory reactions in treated animals 3-fold surpassed the control level ($p<0.01$). In treated rats, the time spent in open arms and the number of hang down movements tended to decrease, while the total number of entries into arms increased. These changes indicated impaired systemogenesis of behavioral reactions, in particular, exploratory activity. In the brain stem of treated animals, norepinephrine concentration was 2-fold lower than in the control, and serotonin was not detected (0). Serotonin concentration in the right cerebral hemisphere of treated rats was 15-fold lower than in the control ($p<0.0001$).

Thus, examination of 40-day-old rats (prepubertal period) showed that prenatal exposure to lead caused neuronal necrosis, which resulted in reduced neuronal density in the neocortex, behavioral disorders, and changes in the content of neurotransmitters, especially serotonin in the brain. The serotoninergic and catecholaminergic systems of the brain in rodents are formed few days before birth and can be affected by various detrimental factors, including serotonin [8,10]. It can be assumed that sharp decrease in serotonin concentration is due to lead-induced damage to serotoninergic neurons during critical period of their develop-

TABLE 1. Effects of Lead Administered to Pregnant Rats on Their Offspring (*M*±*m*)

Parameter	Group	
	control	experiment
Body weight, g	88±2.7	102±2.7*
Weight of brain, mg	1518±25	1513±26
mg/g body weight	17.4±0.49	14.7±0.34*
Width of cortex, μ		
anterioparietal cortex	1569±41.2	1525±29.8
parietal cortex	1130±16.2	1108±31
Width of layer I, μ		
anterioparietal cortex	142±8.8	137±9
parietal cortex	132±8.0	133±6.0
Number of neurons in layer V per vision field		
anterioparietal cortex	16.3±0.6	14.3±0.8
parietal cortex	19.3±1.0	11.3±0.6*
Brain concentration, μg/g		
epinephrine		
hemisphere	0.014±0.0045	0.031±0.0128
brain stem	0.0309±0.0132	0.021±0.0068
norepinephrine		
hemisphere	0.0144±0.068	0.0268±0.0046
brain stem	0.110±0.0229	0.051±0.0091*
dopamine		
hemisphere	0.752±0.1457	0.586±0.0597
brain stem	2.908±0.6634	0.974±0.1377
histamine		
hemisphere	0.588±0.346	0.370±0.109
brain stem	2.13±1.15	0.916±0.227
serotonin		
hemisphere	1.646±0.4375	0.110±0.069*
brain stem	1.101±0.2937	0*

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

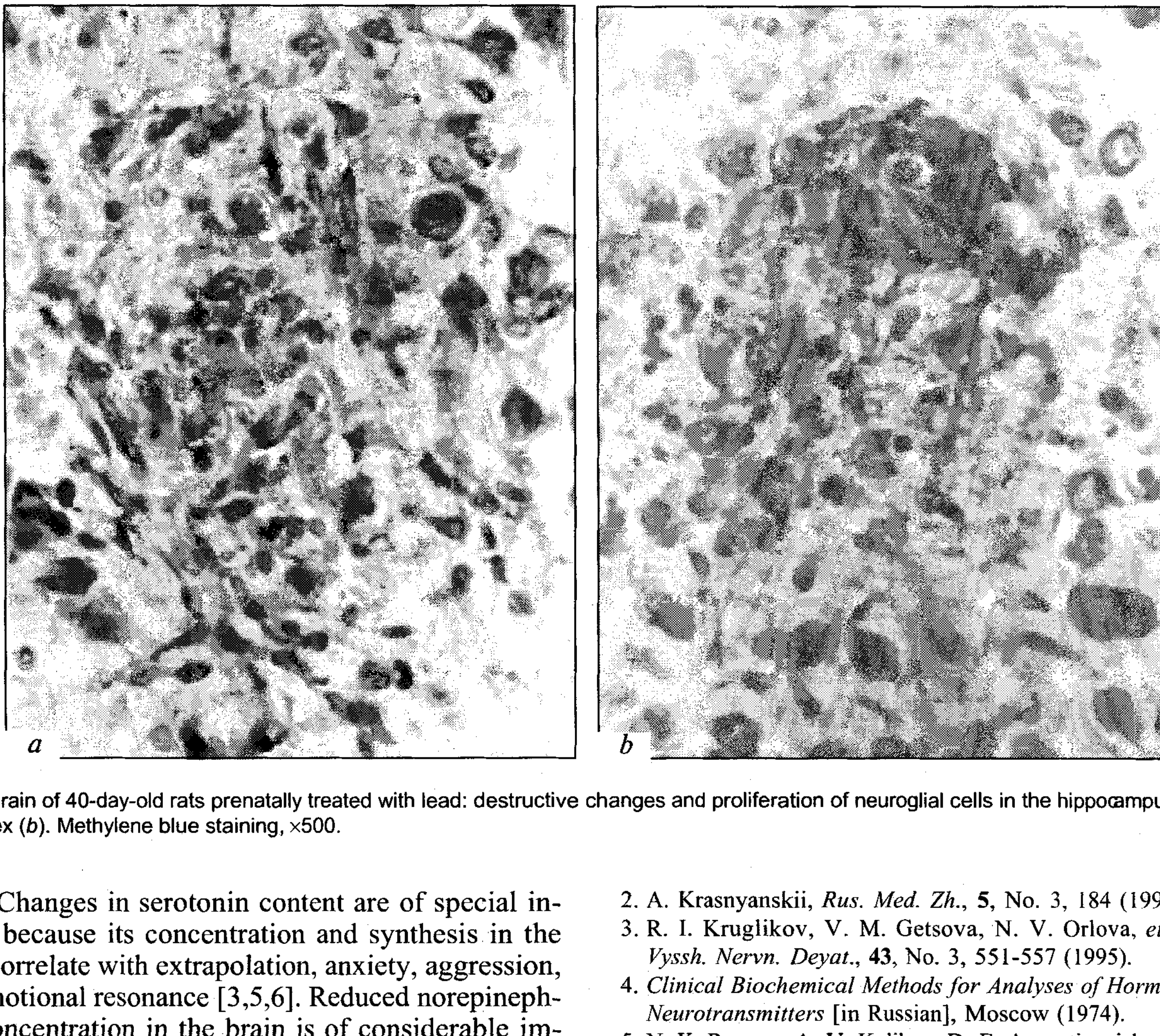

Fig. 1. Brain of 40-day-old rats prenatally treated with lead: destructive changes and proliferation of neuroglial cells in the hippocampus (*a*) and neocortex (*b*). Methylene blue staining, ×500.

ment. Changes in serotonin content are of special interest, because its concentration and synthesis in the brain correlate with extrapolation, anxiety, aggression, and emotional resonance [3,5,6]. Reduced norepinephrine concentration in the brain is of considerable importance, because it determines dominant behavior and extrapolation in animals [6,7].

Our findings are of considerable importance because lead is a widely distributed anthropogenic toxicant. The offspring of females treated with lead by this procedure can be used in elaborating new methods for the prevention and correction of impaired brain development.

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