Polish Journal of Environmental Studies Vol. 11, No. 4 (2002), 307-314

Effect of Organic Mercury Exposure During Early Stage of Ontogenic Development on the Central Dopaminergic System in Adult Rats

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Received: 4 January, 2002
Accepted: 13 February, 2002

Abstract

Organic mercury (CH_3HgCl) with metal concentration 5 ppm in tap water was applied to rats suckling their newborn for the first 21 days of life. A second group of young rats took the mercury in their tap water 5 ppm from the 22nd to the 43rd day of postnatal life. Control rats drank tap water only. In 2-month-old male rats the following behavioral study was performed after saline or specific central dopamine receptor agonists and agonists apply (quinpirole, SKF-38393, haloperidol, SCH-23390): irritability, yawning behavior, oral activity, locomotion, exploratory activity, and catalepsy. In the striatum and frontal cortex of three examined groups the biogenic amines levels (DA, DOPAC, HVA, 3-MT, 5-HT, 5-HIAA, NA) were estimated by means of HPLC/ED technique, and DA and 5-HT turnover.
The effect of quinpirole (a central dopamine D_2 receptor agonists) was also examined on (^{3}H)glucose uptake in discrete parts of the brain. It was shown that mercury affected behavioral changes after dopaminergic agents apply to adult animals when exposed in the period from the 22nd to 43rd day of postnatal development. Biochemical changes (biogenic amines level, turnover and (^{3}H)glucose uptake) were more pronounced in adult animals exposed to mercury via mother's milk (1st to 21st day of life). In light of the above we conclude that early postnatal exposure of rats to organic mercury modulates activity of the central dopamine neurotransmitter system.

Keywords: rats, CH_3HgCl, behavior, biogenic amines, (^{3}H)glucose uptake

Introduction

Mercury is a highly neurotoxic agent in both animals and humans. It is a contaminant of the environment due to its natural abundance and industrial use. For centuries it was an ingredient of drugs such as diuretics, antibacterials, antiseptics, skin ointments and laxatives. Mercury also has a number of industrial uses; therefore, poisoning from occupational exposure and from environmental pollution continues to be an area of concern. Mercury exists in a metallic form (elemental mercury) and as salts, in two states of oxidation: as monovalent mercurous inorganic salts (e.g. mercurous chloride, or calomel) or as divalent mercuric salts (such as organic compounds). The first serious medical signal concerning mercury

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intoxication originated in the city of Minamata Gay in Japan, where residents were poisoned by methyl mercury after eating local poisoned fish [9, 10, 17]. Other incidents of human poisoning from the inadvertent consumption of mercury-treated grains have occurred in Pakistan, Ghana and Guatemala, with a very serious outbreak occurring in Iraq in 1972, where alkyl-mercury salts were used as fungicides [5].

Toxic effects of mercury in humans depend on the chemical form of the metal digested, and on length of exposure. Elemental mercury is not particularly toxic when swallowed, because of its low absorption from the gastrointestinal tract. However, inhaled mercury vapors are absorbed through the lungs, and then oxidized in the erythrocytes by catalase to form toxic compounds [30]. Gastrointestinal absorption of inorganic salts of mercury is approximately 10% of the amount ingested, while organic salts are much better absorbed (90%), because they are lipid soluble [20]. Another source for mercury in the body are dental amalgams [6]. Mercury can be released mostly during chewing and inhaled or absorbed in the gastrointestinal tract and transferred to the different tissues and organs, and also passed to the milk.

The major effects of mercury in humans are nephrotoxic and neurotoxic [20] as mercury and organic salts easily cross the blood-brain barrier [18]. Clinical manifestations of neurotoxic effects are parathesia, ataxia, neurasthenia, vision and hearing loss, spacity and tremor, and consequently coma and death.

Prenatal and early periods of postnatal life are the most sensitive stages for mercury intoxication, and were firstly identified by Warkany and Hubbard [38] as acrodynia ("Pink Disease"). All forms of mercury easily cross the placenta, and concentration of the metal in fetal tissues is the same or even higher as in selected tissues of maternal origin, such as erythrocytes and brain [25, 34]. Mercury is also easy excreted to milk, a source of metal for suckling babies. Developing central nervous systems in mammals is supersensitive to the toxic effects of mercury [39], and many macroscopic and microscopic abnormalities in brains of children and of animals are related to intrauteral mercury exposure. Data on the effects of mercury on central neurotransmitters' systems, mostly dopaminergic and cholinergic, is scarce [11].

Previously we examined the effect of exposure of pregnant rats to inorganic salt of mercury ($HgCl_2$) 50 ppm in their drinking water on the central dopamine system in adult offspring [19, 33]. The aim of the present study was to examine the effects of methyl mercury exposure on the reactivity of the central dopaminergic system and biogenic amine levels in adult rats that had been exposed to mercury during two periods of postnatal life via mother's milk (1st to 21st day of postnatal life) or in their drinking water from the 22nd to 43rd day of life. Since glucose is the major source of energy for the body, uptake of tritiated glucose in those animals was also examined.

Material and Methods

Rats and schedule. Pregnant Wistar rats weighing 200-220 g each were used in the present study. The rats were housed in a well-ventilated room, thermostated to 22 ± 2°C, and under a 12 h light: 12 h darkness cycle, and got free access to pelleted food (Altromin, Lage, Germany) and tap water. The local Bioethic Committee for Animal, Medical University of Silesia approved the experiments. All animals tested were carried out in accordance with NIH regulation of animal care, as described in "Principles of laboratory animal care".

From the first day of their delivery rats started to drink tap water containing 0 (control) or 5 ppm methyl mercury chloride, CH_3HgCl (Sigma Chemicals, St. Louis, MO, USA). Offsprings stay with mother till the 21st day of postnatal life, and by this were exposured to mercury via mother's milk mostly. Righting reflex and time of eye opening of the newly born pups was controlled daily. On the 22nd day male rats were separated from their mothers and kept three per cage until 2 months old. During this time they got free access to pelleted food and tap water.

The third group of 22-day-old male rats started to drink tap water with CH_3HgCl containing 5 ppm of mercury for the next 3 weeks (till the 43 day of life). Then rats started to drink tap water only. All behavioral and biochemical examinations (except righting reflex and eye opening) were performed when animals reached 2 months.

Behavioral Study

Righting reflex. Each rat was repeatedly placed on its back. When the rat managed to fully rotate, and to place its four paws on the grid, we defined it as "reflex was developed". This procedure was performed each day, starting from the first day of postnatal life, until the day when all rats acquired this reflex.

Time of eye opening. Each day, starting on the 10th postnatal day, each rat was examined for eye opening, and the percent of rats with open eyes was recorded. The last examination was performed when all rats exhibited open eyes.

In two-month-old male rats of three groups (exposured to mercury from 1st to 21st day of postnatal life - mostly via mother's milk, exposed from 23rd to 43rd day of postnatal life via drinking water and control) the following behavioral parameters were measured:

Irritability was evaluated according to Nakamura and Thoenen [32].

Yawning behavior was evaluated by administration of quinpirole, according to Kostrzewa and Brus [21, 22]. Rats were placed in individual transparent cages in a quiet, well-ventilated and well-illuminated room. They were allowed to acclimatize to the lab environment for one hour, and then each rat was injected IP with saline, 1 ml/kg. The number of yawns per rat were counted for exactly 60 minutes, and then each rat was injected IP with a low dose (0.0125 mg/kg) of quinpirole, a selective central D_2 receptor agonist, and was observed for an additional 60 minutes. The same male rats were challenged on subsequent days with increasing doses of quinpirole: 0.025, 0.05 and 0.1 mg/kg, one dose per day, and were observed the same way. Quinpirole is known to be associated with selective induction of yawning activity in rats [21].

Oral activity was evaluated by SKF-38393 (a selective central Di receptor agonist) as reported [13, 23]. The rats were allowed to acclimatize in their transparent cages as above, and were injected IP with saline, 1.0 ml/kg. The number of oral movements (chewing episodes) was counted for one minute every 10 minutes, over a period of 60 minutes, beginning 10 minutes after saline injection. Then each rat was injected IP with a low dose (0.03 mg/kg) of SKF-38393 and observed for an additional 60 minutes as above. The same rats were challenged IP on subsequent days with increasing doses of SKF-38393 (0.1, 0.3 and 1.0 mg/kg), and were observed the same way.

Locomotor activity. Rats were individually placed in transparent glass cages 48x26x36 cm, and were allowed to acclimatize for 30 minutes. Then 1.0 ml/kg saline was injected IP to rat of each group, and 10 minutes later locomotor activity (time each rat spent walking, sniffing, grooming and rearing) was recorded in seconds, during 10 minutes. After completing the observation, rats were injected IP with quinpirole 2.0 mg/kg or with SKF-37393 3.0 mg/kg. Observation of locomotor activity was repeated as above.

Exploratory activity. Rats were injected IP with either quinpirole 2.0 mg/kg IP, SKF-38393 3.0 mg/kg IP or saline 1.0 ml/kg IP. Ten minutes later each rat was placed on the center of a wooden platform, 100 cm square. The flat platform had 4 rows of 4 holes each, 7 cm in diameter and 20 cm apart. The number of times (during a three-minute period) that each rat stuck its head beneath the interaural line, into any hole, was counted and recorded [12].

Cataleptogenic activity was evaluated as described by Kostrzewa and Kastin [24], using 0.5 mg/kg IP of haloperidol, a selective central D_2 antagonist, 0.5 mg/kg IP SCH-23390, a selective central Di receptor antagonist, or saline. Each rat in its turn was placed on a 25x50 cm wire mesh screen, forming lxl cm squares, and inclined by 60° to the horizontal plane. The time (in seconds) taking each rat to move any paw along at least one screen division was recorded, with 60 seconds the maximum time allowed to stay. Results were the sum of five measurements taken at 15, 30, 45, 60 and 90 min after saline 1.0 ml/kg IP, haloperidol 0.5 mg/kg IP or SCH-23390 0.5 mg/kg IP injection.

Glucose uptake. Two-month-old male rats of three examined groups were divided into two subgroups and injected IP with saline 1.0 ml/kg, or with the dopamine agonist quinpirole 2.0 mg/kg. This was followed 15 minutes later by an IP injection of 6-^{3}H-D-glucose (Amersham Radiochemicals, Pittsburgh, PA, USA; 41 Ci/mmol), at a dose of 500 µCi/kg BW. Rats were sacrificed 15 minutes after administering the tritiated glucose. Brains were immediately excised and placed on ice, and the striatum, cerebral cortex, hippocampus, thalamus with hypothalamus and cerebellum separated, weighed and placed in 20-ml scintillation vials. One ml Soluene-350 (Packard Inc., Downers Grove, Ill., USA) was added to each vial, and the tightly closed vials were incubated at 37°C for 38 hours, until the tissues were completely solubilized. In addition, the following tissues were sampled for counting of radioactivity: heart and tongue muscle, liver, kidney, salivatory gland and buccal mucose membrane.

Ten ml of scintillation cocktail (Dimilume-30, Packard Inc., Downers Grove, IL., USA) were then added. The vials were briefly vortexed and counted in a scintillation counter (Liquid Scintillation Counter: DSA 14091, Wallac, Finland). Mean ± SEM of DPM (desintegration per minute) per 100 mg of wet tissue were calculated for each group.

Catecholamine assay. Two-month old male offsprings from all three study groups were sacrificed by guilliotine, and their brains were immediately excised and placed on ice. The striatum and frontal cortex were separated, placed on dry ice, weighed and stored at -70°C, pending assay. Dopamine (DA) and its metabolites 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 3-methoxytyramine (3-MT), and 5-hydroxytryptamine (5-HT), 5-hydroxyindolacetic acid (5-HIAA) and noradrenaline (NA) were assayed by an HPLC/ED technique [28, 37].

Dopamine and 5-hydroxytryptamine turnover. Control and experimental rats were injected with m-hydroxybenyzlhydrazine dichloride (NSD-1015) 100 mg/kg IP (an aromatic amino acid decarboxylase inhibitor) [8]. Thirty minutes later the rats were decapitated, skulls opened and brains excised. Corpus striatum was excised and stored in -70°C until assayed. Then L-dihydroxyphenyl-alanine (L-DOPA) and 5-hydroxytryptophane (5-HTP) were assayed by HPLC/ED [28, 37]. The levels of amino acids were expressed in ng/g of wet tissue, and synthesis rate of DA and 5-HT were calculated in nmol/g/h [8].

Chemicals. Quinpirole, SKF-38393, SCH-23390 and standards samples for biogenic amines assay were purchased from Sigma Chemicals, St. Louis, MO, USA, while haloperidol was bought from Polfa Chem. Co.

Statistical analyses. An analysis of variance (ANOVA) and the post-ANOVA test of Neuman-Keuls were used to test the differences between groups for significance. A "p" value of 0.05 or less was used to indicate a significant difference.

Results

The eye opening of mercury-intoxicated rats was delayed as compared to rats drinking tap water (results not presented).

Irritability in rats that were exposed, from 22nd to 43rd day of postnatal life to 5 ppm mercury in their drinking water, was significantly higher after SKF 38393 3.0 mg/kg IP only, as compared to respective control: 2.44 ± 0.24 vs 1.44 ± 0.29 scores respectively ($p < 0.05$).

Quinpirole induced yawning behavior in a dose-dependent manner, in both control and mercury exposed rats. The number of yawns after quinpirole 0.1 mg/kg IP, in mercury-pretreated rats, was significantly higher as compared to the control and mercury pretreated during first three weeks of postnatal life (Fig. 1).

When SKF-38393 was administered at doses 0.03 and 0.1 mg/kg IP, the number of oral movements increased to a higher extent in mercury exposured during 23rd to 43rd day of postnatal life animals. SKF-38393 1.0 mg/kg IP

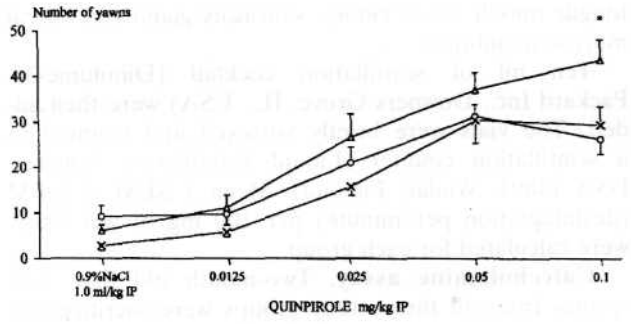

Fig. 1. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on number of yawns induced with quinpirole in adult animals (n = 9).
Explanation: o-o Control; x-x Mercury exposure during lst-21st day of postnatal life; A-A Mercury exposure during 22nd-43rd day of postnatal life.
* $p < 0.05$

induced significantly lower number of oral movements in those rats exposured via mother's milk as compared to control (Fig. 2).

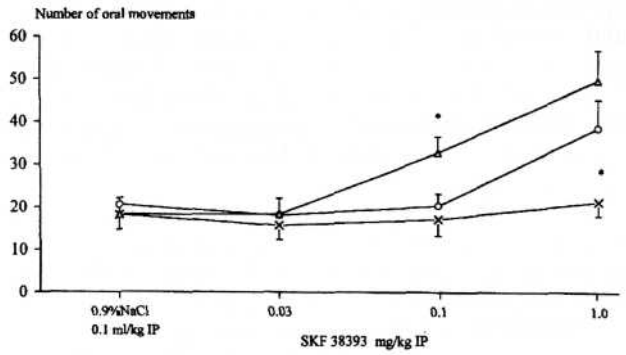

Fig. 2. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on number of oral movements induced with SKF 38393 in adult animals (n = 9). Explanation as in Figure 1.

Locomotion (time in seconds each rat spent walking, sniffing, grooming and rearings during 10 min observation) was significantly higher ($p < 0.05$) in adults exposed to mercury during the first three weeks of postnatal life as compared to exposure via milk and control (243.5 ± 43.7; 188.3 ± 40.6 and 117.1 ± 42.9 seconds respectively). Quinpirole 2.0 mg/kg IP significantly ($p < 0.05$) intensified locomotion in all three examined groups to a higher extent in rats exposed to mercury in the second period of postnatal life (319.4 ± 87.1; 492.1 + 45.3 and 348.0 ± 68.3 seconds respectively; differences significant to respective controls). SKF 38393 3.0 mg/kg IP significantly decreased the locomotion in control and second mercury exposed group of adult rats. (16.5 + 11.6; 49.0 ± 19.6 and 221.1 ± 40.6 seconds respectively).

Exploratory activity (number of peepings during 3 minutes of observation) after saline injection was similar in three examined groups (Fig. 3). Quinpirole 2.0 mg/kg and SKF 38393 3.0 mg/kg IP attenuated this activity, but quinpirole exerted the strongest effect as compared to SKF 38393. Effects were more expressed in the rats exposured to mercury mostly via mother's milk.

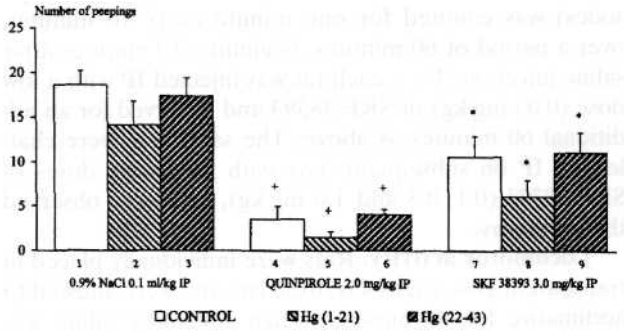

Fig. 3. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on the exploratory activity expressed as a number of peepings during 3 minutes of observation in adult animals (n = 9). * $p <$ 0.05-7/1; 8/2, 9/3; + $p < 0.01$ - 4/1, 5/2, 6/3.

Haloperidol 0.5 mg/kg IP induced similar cataleptogenic effect in all three groups of rats (72.5 ± 10.5; 83.3 + 21.3 and 87.7 ± 15.0 seconds respectively). SCH-23390 0.5 mg/kg IP significantly ($p < 0.05$) increased catalepsy in rats exposed to mercury during 22nd to 43rd day of postnatal life as compared to those exposed via mother's milk and control (201.7 ± 16.6; 155.4 ± 33.8 and 143.4 ± 25.2 seconds, respectively).

In rats exposed to mercury during the first 3 weeks of postnatal life uptake of (^{3}H)glucose in the brain expressed in DPM/100 mg of wet tissue was lower as compare to the control or exposured to mercury in the second period of postnatal life (22nd-43rd day) (Tab. 1). Quinpirole 2.0 mg/kg IP in statistically increased (^{3}H)glucose uptake in all examined parts of the brain only in the rat exposed to mercury via mother's milk (lst-21st day). Quinpirole 2.0 mg/kg IP did not modify (^{3}H)glucose uptake in control and mercury exposed animals during 22nd to 43rd day of postnatal life. In the liver and heart muscle the decreased (^{3}H)glucose uptake was observed in 2-month-old rats exposed to mercury via mother's milk only (Tab. 1). In buccal mucose the decreased (^{3}H)glucose uptake was noticed in the group of rats exposed to mercury in the second period (22nd-43rd day).

Mercury decreased the dopamine, DOPAC and HVA level in the cortex and increased 3-MT level in the striatum of 2-month-old rats exposed during the first 3 weeks of postnatal life as compared to control (Tab. 2). Exposure to mercury during the first 21 days decreased dopamine turnover in the striatum of adult rats (Tab. 3).

Discussion

Mercury is transported through the blood-placenta and blood-milk barriers, and is therefore available to the fetuses and the pups during pregnancy and nursing

Table 1. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on (^{3}H)glucose uptake in the brain and peripheral organs of adult animals (DPM/100 mg of wet tissue; n = 4-5), x ± SEM.

PART OF THE BRAIN	Control		Mercury 1st to 21st day		Mercury 22nd to 43rd day	
	0.9% NaCl 1.0 ml/kg IP	quinpirole 2.0 mg/kg IP	0.9% NaCl 1.0 ml/kg IP	quinpirole 2.0 mg/kg IP	0.9% NaCl 1.0 ml/kg IP	quinpirole 2.0 mg/kg IP
STRIATUM	35715 ± 3528	32750 ± 4160	25661* ± 510	36521* ± 2284	43390 ± 2021	45531 ± 4260
CORTEX	38563 ± 3481	37107 ± 5973	27805* ± 859	38927* ± 1777	44961 ± 1734	45507 ± 475
HIPPOCAMP	34817 ± 2696	32890 ± 4129	25187* ± 1514	37310* ± 1682	44479 ± 3394	50795 ± 3212
THALAMUS WITH HYPOTHALAMUS	38644 ± 3394	34009 ± 4411	26937* ± 906	36682* ± 1703	45456 ± 1767	41743 ± 2475
CEREBELLUM	38156 ± 4443	32640 ± 4378	26295* ± 408	36270* ± 1896	47600 ± 3211	45549 ± 5762
PERIPHERAL ORGAN						
LIVER	43679 ± 7049		35206* ± 1225		44833 ± 8519	
KIDNEY	48512 ± 6622		40049 ± 948		45157 ± 2503	
HEART MUSCLE	47440 ± 4763		38738* ± 1044		44275 ± 9160	
TONGUE MUSCLE	40774 ± 2401		38884 ± 1787		35064 ± 675	
SALIVARY GLAND	38535 ± 603		38600 ± 984		32276 ± 2836	
BUCCAL MUCOSE	45662 ± 6441		39775 ± 1723		34902* ± 2029*	

* $p < 0.05$ as compare to the respective control

respectively, in higher concentrations than in mothers' body [15, 16, 34, 36]. Organic compounds, because their lipophylic properties easily cross the blood-brain barrier, are excreted to milk. Therefore, we selected models of organic mercury intoxication of developing rats in two different periods. The method of exposure was also different. In the first period (1st to 21st day) mostly via mother's milk, and in the second (22nd to 43rd day) straight from tap water. The reason for choosing neurotransmitters-induced behavioral parameters as criteria stems from the fact that the fetal and developing brain is susceptible to the toxic effects of mercury [29], and that the uptake of mercury by the young rat brain is greater than in an adult [1]. It has been demonstrated that mercury interferes with synaptic mechanisms of release of some neurotransmitters, and is responsible for the impairment in various neurotransmitters' systems, such as the GABAergic and cholinergic ones [7, 11, 39].

The central nervous system has a variety of receptor subtypes of the dopamine D_1 and D_2 types. As both types of dopamine receptors are involved in behavioral, neurological and psychotic disorders, many of their agonists and antagonists have been used for treating mental disturbances. In addition, selective agonists such as SKF-38393 and quinpirole, and antagonists such as haloperidol and SCH-23390, have been widely used as pharmacological tools. SKF-38393 is an agonist of the Di receptor-induced oral activity in rats [23, 31]. Quinpirole is an agonist of the D_2 receptor, which is involved in yawning activity [21]. For this reason we have used the oral activity and yawning parameters induced by dopamine agonists, for assessing the reactivity of dopamine receptors following prenatal exposure to mercury.

The present study indicates that reactivity of D_2 receptor in the rats that had been exposed to 5 ppm mercury mostly during the later period of development increased to the dose of the activating drug quinpirole, but only in the highest dose used. SKF-38393 (being an agonist of the D_1 receptor) also induces greater reaction in animals exposed to mercury during 22nd to 43rd postnatal day. In animals exposed to mercury via mothers' milk reactivity to SKF 38393 was lower as exposed as oral activity. There were also differences between control and mercury-pretreated rats in locomotor and exploratory activities after administration of dopamine agonists. In addition, mercury caused changes in DA, DOPAC, HVA and 3-MT levels in selected parts of the brain of animals exposed with mercury during the first 21 days of postnatal life, only.

There is not too much data concerning the effect of mercury on the central dopaminergic system. Reynolds and Pitkin [34] reported that $HgCl_2$, 4 mg/kg/day, administered orally to rats from their 2nd to 60th day of postnatal life, caused an increase in DA and NA, and decreased acetylcholine levels in selected parts of the brain, but not in the striatum. When mercury was applied during the first three weeks of postnatal life, a decreased uptake of labeled DA and NA in brain synaptosomes was noticed [34].

Inhalation of mercury vapors decreases locomotor and exploratory activities, and the ability of learning different tasks in rats *[2,* 3]. Lehotzky et al. [26] administered methoxy-ethyl-mercury chloride 2.0, 0.62 or 0.02 mg/kg orally to rats between 7-15 days of their pregnancies, and reported on the 90th day of age of their offsprings, a decrease in their ability to learn passive avoidance reflex. Similar results were reported by others

Table 2. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on biogenic amines level in the brain of adult animals (ng/g of wet tissue; n = 5-6), x + SEM.

Amine	Part of the brain	Control	Mercury 1st to 21st day	Mercury 22nd to 43rd day
DA	STRIATUM	11078.8 ± 368.2	12055.5 ± 645.4	10778.2 ± 525.9
	CORTEX	394.6 ± 65.3	197.3* ± 45.7	380.7 ± 64.1
DOPAC	STRIATUM	881.8 ± 73.9	890.2 ± 34.1	871.3 ± 47.9
	CORTEX	39.6 ± 4.3	24.6* ± 3.1	44.6 ± 5.2
HVA	STRIATUM	598.7 ± 29.0	634.8 ± 37.3	587.9 ± 33.5
	CORTEX	80.5 ± 6.0	57.8* ± 4.0	90.1 ± 9.4
3-MT	STRIATUM	120.5 ± 12.7	182.1* ± 9.0	116.6 ± 5.5
	CORTEX	–	–	–
5-HT	STRIATUM	506.0 ± 29.7	472.6 ± 12.8	483.1 ± 21.9
	CORTEX	382.9 ± 25.4	379.0 ± 22.6	423.0 ± 14.4
5-HIAA	STRIATUM	580.8 ± 26.7	637.4 ± 41.4	561.1 ± 25.5
	CORTEX	183.6 ± 11.6	183.1 ± 11.3	207.8 ± 9.6
NA	STRIATUM	90.2 ± 9.8	74.5 ± 3.9	91.1 ± 10.7
	CORTEX	170.5 ± 8.6	160.7 ± 14.0	185.0 ± 13.9

* $p < 0.05$ as compare to the control

Table 3. Effect of mercury 5 ppm exposure in different periods of postnatal life of rats on L-DOPA and 5-HTP level (ng/g of wet tissue), and dopamine (DA) and 5-hydroxytryptamine (5-HT) turnover in the brain's striatum of adult animals (nmol/g of wet tissue/1 hour; n = 5-6), x ± SEM.

Amino acid	Part of the brain	Control	Mercury 1st to 21st day	Mercury 22nd to 43rd day
L-DOPA	STRIATUM	1572.2 ± 87.2	1178.3* ± 38.0	1336.9* ± 62.2
	CORTEX	117.3 ± 3.8	122.3 ± 5.0	116.5 ± 7.2
5-HTP	STRIATUM	223.9 ± 18.5	210.8 ± 14.3	221.4 ± 13.4
	CORTEX	95.9 ± 6.6	105.5 ± 8.4	102.5 ± 11.7
AMINE	AMINE TURNOVER			
DA	STRIATUM	15.94	11.95	13.55
	CORTEX	1.18	1.24	1.18
5-HT	STRIATUM	2.13	1.91	2.01
	CORTEX	0.87	0.95	0.93

* $p < 0.05$ as compare to the control

[35]. Cuomo et al. [11] tested 22-day-old offspring of mothers that had been exposed prenatally to mercury, and recorded increased locomotor activity after apomorphine administration. They also recorded increased binding of ^{3}H-spiperone in the striatum. This latter fact can be explained by an increase in DA receptor density in the brain of rats prenatally exposed to mercury, which in turn is expressed as supersensitivity of dopamine receptors. Our present and previous findings [19, 33] partially confirm the above-cited results, suggesting that early postnatal exposure to mercury changes the functions of the central dopamine system in adult rat.

Molecular mechanisms of mercury's neurotoxic effect is intensively examined. Its reaction with sulfur groups of many enzymes also disturbs nucleic acid synthesis [14]. Mercury induces free oxygen radical formation, which are cytotoxic [27]. In the neurotoxic mechanism of mercury, astrocytes seems to play an important role. They are first in the brain where metal is cumulated and then influence negatively on development of neurons and their function [4].

Glucose is a main source of energy for the brain and some peripheral tissues. In the present study we have noticed that rats exposed to mercury in the early period

of postnatal life (1st to 21st day) did affect glucose uptake in the brain and in some peripheral tissues of adult rats. The central neuronal system, kidney, and liver are targets for the toxic effects of mercury, as this metal cumulates in them [20, 29]. An agonist of the central dopamine receptor - quinpirole, modified the glucose uptake in examined parts of the brain and confirmed the changes in activity of the central dopaminergic system after exposure to mercury. This also confirms our previous study where prenatal exposure of rats with inorganic mercury ($HgCl_2$) also changed (^3H)glucose uptake in adult offspring, when agonist of the central dopamine D_3 receptors 7-OH-DPAT was applied [33]. From above we conclude that early postnatal exposure of rats to organic mercury modulate activity of the central dopamine neurotransmitter system.

Acknowledgements

This study was supported by grant No. NN-2-061/01 awarded by the Medical University of Silesia (RB). The authors wish to thank Mrs. U. Mikolajun, W. Tramer and B. Medrek for their excellent technical assistance, and Ms. M. Gajdzik for preparing the manuscript.

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