SELECTIVE EFFECT OF CHRONIC LEAD INGESTION
II : EFFECT ON PHENYLETHANOLAMINE
N-METHYLTRANSFERASE ACTIVITY IN
BRAIN REGIONS OF RATS

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ABSTRACT — Selectivity of lead effect to phenylethanolamine N-methyltransferase (PNMT) activity in regions of brain from rats postnatally exposed to lead was tested. Three groups of animals were prepared; (1) Rats exposed to lead at a low dose (0.05% PbAcetate : PbAc); (2) Rats exposed to lead at a high dose (0.2% PbAc); (3) Age-matched normal control rats. At 2, 4, 6 and 8 weeks of age weight of whole brain and body in each group were measured. At the same ages activities of PNMT and Na⁺/K⁺-ATPase were examined on 4 brain regions of each animal. Exposure of rats to lead generally decreased activity of Na⁺/K⁺-ATPase and showed alternative change of those of PNMT. Brain regions where changes of PNMT activity were detected without concomitant changes of Na⁺/K⁺-ATPase activity, were telencephalon and pons/medulla at 2 weeks of age and telencephalon at 4 weeks of age in rats exposed to lead at a low dose, and those in rats exposed to lead at a high dose were pons/medulla at 8 weeks of age. These data imply that adrenergic nervous system in the brain regions described above could selectively be affected by lead.

Key words: lead toxicity, phenylethanolamine N-methyltransferase, Na⁺/K⁺-ATPase, selectivity, brain, rat.

INTRODUCTION

Lead is known to induce various toxicities to various nervous systems, kidney, heme-hemoprotein system, gastrointestinal system, re-

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productive system (Fowller et al., 1980; Gross et al., 1975; Needman, 1980; Seppalainen et al., 1975). Most of all, toxicity to central nervous system (CNS) is known to be critical, common and more serious in young experimental animal and man (Frobes and Reina, 1972; Michaelson and Sauerhoff, 1974). The result of neurotoxicity of lead is continuous and irreversible and has
been reported to be morphological changes (Goldstein et al., 1974; Holtzman et al., 1978) and behavioral abnormalities (David et al., 1972; Michaelson and Sauerhoff, 1974; Silberfeld and Goldberg, 1973). On chronic lead intoxication to rodents, it is reported that the activities of central noradrenergic nervous system and dopaminergic nervous system increase (Golter and Michaelson, 1975; Kruk, 1973; Memo et al., 1981) and that of cholinergic nervous system decrease and that of GABAergic nervous system changes (Silberfeld et al., 1980). There are some variabilities between studies on the effect of lead intoxication in the postnatal rats (Shin and Hanin, 1978).

Through the existing literatures indicate that abnormalities in several nervous systems including catecholaminergic, serotonergic and cholinergic nervous system play a pathological role in animals exposed to lead, however, difference of the roles of several nervous systems in causing toxicity by lead has not been clearly elucidated.

It is reported that central catecholaminergic nervous system plays an important role in behavior and emotion of mammals (Joseph and Seymour, 1967; Marvin, 1985; Remond and Murphy, 1975; Shaywitz et al., 1977).

There are possibilities that in postnatally lead-exposed rats abnormalities in central adrenergic nervous system were produced by a selective action on that nervous system or by a nonselective action on all the CNS tissues. The purpose of the present study is to elucidate this issue. In this study, as an index of lead toxicity to central adrenergic nervous system, the activity of PNMT was measured which is located in central adrenergic nervous system and as an index of lead toxicity to all the nonspecific CNS tissues, the activity of Na\(^+\)/K\(^+\)-ATPase was measured which is located in all the tissues of brain.

MATERIALS AND METHODS

Experimental design: Animals were divided into three groups using Wistar rat pups. Each group consisted of almost same numbers of both male and female rats. The first group postnatally received lead acetate at low concentration (0.05%) for up to 8 weeks. The second group postnatally received lead acetate at high concentration (0.2%) for up to 8 weeks. The third group received the same treatment as the first and the second groups without lead acetate. Each group was divided into 4 sub-groups, and activities of PNMT and Na\(^+\)/K\(^+\)-ATPase, brain and body weights were determined in each sub-group; the first sub-group at 2 weeks of age, the second at 4 weeks of age, the third at 6 weeks of age and the last at 8 weeks of age, respectively.

Materials: Ouabain, Trisma base, Tris-ATP, defatted bovine serum albumin, Folin-Ciocalteu reagent, phenylethanolamine, Triton X-100 were purchased from Sigma Chemical Co. (St. Louis, Mo., U. S. A.). S-Adenosyl-L-[methyl-\(^3\)H] methionine (specific activity; 15 Ci/mmol) was purchased from Amersham Shearle (Clearwater, Ill., U. S. A.) and all the inorganic and organic chemicals were reagent grade. The water used in this experiment was the deionized, double-distilled water.

Animals: Wistar rat pups of both sexes were used. Male and female rats supplied from the Laboratory Animal Center of Seoul National University were mated at 10 weeks of age. Pregnant rats were selected and caged individually.

Within 1 day from parturition, dams nursing their pups were given drinking water containing 0.2% or 0.05% of PbAc, ad libitum.

After weanlings, rat pups continued to receive drinking water containing 0.2% or 0.05% of PbAc throughout the experiment. In all cases number of litters nursed by each dam was equalized to ten in order to minimize differences of nutritional effect during the period of nursing. For example, if one pregnant rat delivered twelve litters and the other eight, two litters among twelve delivered by the first rat were removed from their dam and transferred to the second rat for nursing which delivered only eight litters. All pups were separated from their dams at 3 weeks after birth. Rat pups in the control group received normal tap water. Animals were sacrificed by decapitation between 9 and 10 A. M. of the day when animals became 2, 4, 6 and 8 weeks of age. Brains were rapidly removed from animals and dissected by the method of Glowinski and Iverson (1966) into four anatomical regions: telencephalon, diencephalon, midbrain and pons/
medulla.

**Determination of Na\(^+\)/K\(^+\)-ATPase activity**: The activity of Na\(^+\)/K\(^+\)-ATPase was assayed by the method of Silva et al. (1973) using microsomal fraction which was prepared by the method of Morgan and Matthews (1971). The brain regions were homogenized with tissuehomizer (Tekmar Co., OH., U. S. A.) set at 60 in 10 volumes of solution (w/v) containing 0.32 M sucrose, 2.4 mM sodium deoxycholate, 2 mM EDTA and 50 mM Tris-HCl buffer (pH 7.4). The homogenates were centrifuged at 14,000×g (15 min, 4°C) and the supernatants obtained were centrifuged at 70,000×g (10 min, 4°C). The pellet was suspended by adding medium containing 0.32 M sucrose, 20 mM EDTA and 50 mM Tris-HCl buffer (pH 7.4) enough to bring the final protein concentrations to 0.4–0.5 mg/ml. All samples were stored at −70°C until used for assays.

Na\(^+\)/K\(^+\)-ATPase activity was determined by subtracting Mg\(^++\)-ATPase activity (ouabain-insensitive) from total ATPase activity. The medium used for estimation of total ATPase activity consisted of final concentrations (mM) of: Tris-HCl buffer (pH 7.4), 50; MgCl\(_2\), 5; KCl, 3; NaCl, 100; and 0.2 ml of enzyme suspension which was stored. Mg\(^++\)-ATPase activity was measured in the above medium without NaCl and KCl and containing 0.1 mM ouabain. In all experiments reaction mixture was preincubated in shaken-water bath for 10 min at 37°C. The reaction was started by addition of 5 mM Tris-ATP and incubated in a water bath at 37°C. After 20 min, reaction was stopped by adding 1 ml of 10% trichloroacetic acid in an ice bath, and centrifuged for 10 min at 4°C. The inorganic phosphate liberated was measured by the method of Lebel et al. (1978). To 0.2 ml of supernatant, 0.6 ml of copper acetate (0.25% CuSO\(_4\) and 4.6% NaAc in 2 N acetic acid, pH 4) and 0.1 ml of 5% ammonium molybdate were added and mixed rapidly. Then, 0.1 ml of 2% Elon in 5% sodium sulfite was added and mixed. Seven minutes later, the absorbance was read at the 870 nm using spectrophotometer (LKB, Biochrom., UK). The activity of enzyme was expressed as micromoles of inorganic phosphate liberated per milligram of protein per hour.

**Determination of PNMT activity**: For PNMT activity determination a modification of the method of Saavedra et al. (1974) and Petty and Reid (1979) was used. Each tissue prepared was homogenized in 5 volumes (w/v) of ice-cold 0.2 M Tris-HCl buffer (pH 8.6), containing 0.2% (v/v) Triton X-100, with glass and teflon homogenizer, and centrifuged at 1250×g for 10 min at 4°C. The supernatant served as the enzyme source to determine the activity of PNMT. In ice-cold 13 ml stoppered centrifuge tubes, 94 μl deionized double-distilled water, 5 μl of 1 mg/ml solution of phenylethanolamine in water and 1 μl of [\(^3\)H]-SAM were placed and mixed well. After the addition of 100 μl supernatant into the reaction tubes, the tubes were incubated for 30 min, at 37°C. Blanks were prepared by the addition of denatured enzyme source to substrate mixture. The reaction was terminated by the addition of 0.6 ml of 0.5 M borate buffer (pH 10) and 6 ml of 3% isoamyliccohol in toluene was added. The reaction tubes were then vigorously vortexed for 30 sec. A 5 ml aliquot of the organic layer was transferred to a scintillation counting vial and the solvent was evaporated to dryness in vacuum drying oven. A 10 ml of scintillation cocktail was added to the residual product and counted by liquid scintillation counter (LKB, Biochrom., UK). PNMT activity was expressed as picomoles of produced N-[\(^3\)H]-methylated phenylethanolamine per mg protein per hour.

**Protein assay**: Protein content was measured by the method of Lowry et al. (1951). Bovine serum albumin was used as standard.

**Data analysis**: Activities of Na\(^+\)/K\(^+\)-ATPase and PNMT were examined by analysis of variance (ANOVA) in each brain region for a given condition with time after compared means from exposed (to lead either at low or high concentration) and control groups in animals. When ANOVA indicated the presence of a significant exposure effect, standard test was used to compare means from exposed and control animals to determine the basis of the difference.

**RESULTS**

Whole brain weight gain was significantly decreased at 4 and 6 weeks of age in rats exposed to low and high dose of lead as illustrated in Fig.
**Fig. 1.** Whole brain weight of postnatally lead-exposed rats. Low: rats received 0.05%, and High: 0.2% of lead acetate through drinking water. Each point represents the mean ± S. D. of the data from 4-5 animals. *: Indicates a significant difference from control group (P<0.05).

**Fig. 2.** Body weight of postnatally lead-exposed rats. Low: rats received 0.05%, and High: 0.2% of lead acetate through drinking water. Each point represents the mean ± S. D. of the data from 4-5 animals. *: Indicates a significant difference from control group (P<0.05).
Table 1. PNMT activity in brain regions of CNS of postnatally lead-exposed rats.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Group</th>
<th>2 Weeks of Age</th>
<th>4 Weeks of Age</th>
<th>6 Weeks of Age</th>
<th>8 Weeks of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>TELENCEPHALON</td>
<td>Control</td>
<td>7.07±0.58</td>
<td>10.71±1.66</td>
<td>13.33±0.97</td>
<td>13.69±0.44</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>5.58±0.85*</td>
<td>7.54±1.13*</td>
<td>12.12±1.08</td>
<td>11.41±1.01*</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>4.43±1.12*</td>
<td>8.83±0.58</td>
<td>10.16±1.87*</td>
<td>12.56±0.32*</td>
</tr>
<tr>
<td>DIENCEPHALON</td>
<td>Control</td>
<td>4.95±0.41</td>
<td>7.35±1.13</td>
<td>5.23±0.56</td>
<td>6.45±1.13</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>5.85±0.68*</td>
<td>5.82±0.97</td>
<td>5.93±1.29</td>
<td>6.57±1.06</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>4.18±0.67</td>
<td>5.82±0.67*</td>
<td>5.57±0.32</td>
<td>4.65±0.45*</td>
</tr>
<tr>
<td>MIDBRAIN</td>
<td>Control</td>
<td>5.50±0.61</td>
<td>5.52±0.63</td>
<td>5.56±0.86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>4.93±0.87</td>
<td>4.87±0.61</td>
<td>4.04±0.43*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>4.76±0.63</td>
<td>4.89±0.79</td>
<td>4.06±0.23*</td>
<td></td>
</tr>
<tr>
<td>PONS / MEDULLA</td>
<td>Control</td>
<td>21.33±2.84</td>
<td>20.08±2.12</td>
<td>19.72±1.35</td>
<td>20.28±3.54</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>25.97±1.87*</td>
<td>21.71±1.99</td>
<td>18.65±1.68</td>
<td>16.91±1.89</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>14.99±1.86*</td>
<td>16.77±2.05*</td>
<td>13.47±2.57*</td>
<td>9.71±1.89*</td>
</tr>
</tbody>
</table>

Each value represents the mean ± S.D. of data from 5 animals.
* : Indicates a significant difference from control group (P<0.05).
** : Data for midbrain at 2 weeks of age are represented by those for diencephalon since assays were carried out using both tissues unseparated.

1. Body weight gain in Fig. 2 was significantly decreased at 4, 6 and 8 weeks of age in rats exposed to low and high dose of lead.

The effect of lead ingestion to rat pups on PNMT activity from birth in various brain regions is summarized in Table 1. Brain regions which exhibited a significant change in PNMT activity in rats exposed to low dose of lead were telencephalon, diencephalon+midbrain and pons/medulla at 2 weeks of age, telencephalon at 4 weeks of age, telencephalon and midbrain at 8 weeks of age, and those in rats exposed to lead at high dose were telencephalon and pons/medulla at 6 weeks of age, telencephalon and diencephalon, midbrain and pons/medulla at 8 weeks of age.

The effect of exposure of pups to lead on Na⁺/K⁺-ATPase activity in various brain regions is summarized in Table 2. The activity of Na⁺/K⁺-ATPase was consistently increased in all groups with age. In lead-exposed rats the activity of Na⁺/K⁺-ATPase was in all cases lower than that of control group. Brain regions which exhibited a significant decrease in Na⁺/K⁺-ATPase activity in rats exposed to lead at a low dose were diencephalon+midbrain at 2 weeks of age, telencephalon and midbrain at 8 weeks of age, and those in rats exposed to lead at a high dose were telencephalon, diencephalon+midbrain and pons/medulla at 2 weeks of age, telencephalon, diencephalon and pons/medulla at 6 weeks of age, telencephalon, diencephalon and midbrain at 8 weeks of age.

The effects of postnatal exposure of pups to lead on activities of PNMT and Na⁺/K⁺-ATPase are summarized for comparison in Tables 3 and 4.

Brain regions where changes of activities were detected not for Na⁺/K⁺-ATPase but for PNMT were telencephalon and pons/medulla at 2 weeks of age and telencephalon at 4 weeks of age in rats exposed to lead at a low dose, and those in rats exposed to lead at a high dose were pons/medulla at 8 weeks of age, respectively.

**DISCUSSION**

The effects of lead on brain weight gain and body weight gain were observed at 4 and 6 weeks of age in rats exposed to low and high dose of lead, at 4, 6 and 8 weeks of age in rats exposed to low and high dose of lead, respectively. Decrease in brain weight gain and body weight gain were taken as the sign of lead toxicity in animals, since there were no changes of mortality as a
Table 2. Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activities in brain regions of postnatally lead-exposed rats.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Group</th>
<th>2 Weeks of Age</th>
<th>4 Weeks of Age</th>
<th>6 Weeks of Age</th>
<th>8 Weeks of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>TELENCEPHALON</td>
<td>Control</td>
<td>10.06±0.96</td>
<td>12.39±1.52</td>
<td>17.09±1.89</td>
<td>21.05±2.35</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>9.04±0.76</td>
<td>11.14±1.30</td>
<td>14.82±2.04</td>
<td>17.53±1.79*</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>7.66±0.66*</td>
<td>10.12±0.95*</td>
<td>14.02±1.07*</td>
<td>16.07±1.46*</td>
</tr>
<tr>
<td>DIENCEPHALON</td>
<td>Control</td>
<td>11.95±1.14</td>
<td>13.43±1.65</td>
<td>20.12±1.86</td>
<td>22.88±3.34</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>9.65±1.05*</td>
<td>12.13±1.00</td>
<td>18.53±1.23</td>
<td>19.73±1.96</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>9.20±1.04*</td>
<td>10.27±0.92*</td>
<td>16.01±2.07*</td>
<td>17.44±1.77*</td>
</tr>
<tr>
<td>MIDBRAIN</td>
<td>Control</td>
<td># #</td>
<td>16.01±2.44</td>
<td>21.97±2.78</td>
<td>26.28±3.15</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>14.04±1.61</td>
<td>19.99±1.32</td>
<td>22.09±2.14*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>13.64±1.22</td>
<td>18.96±1.93</td>
<td>20.29±2.35*</td>
<td></td>
</tr>
<tr>
<td>PONS / MEDULLA</td>
<td>Control</td>
<td>12.57±1.72</td>
<td>13.91±1.76</td>
<td>20.15±2.09</td>
<td>23.22±2.56</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
<td>10.91±1.34</td>
<td>12.50±1.22</td>
<td>17.38±2.26</td>
<td>21.01±2.32</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>9.94±1.01*</td>
<td>11.51±1.50*</td>
<td>16.57±1.47*</td>
<td>20.39±2.09</td>
</tr>
</tbody>
</table>

Each value represents the mean ± S.D. of data from 5 animals.

* : Indicates a significant difference from control group (P<0.05).

##: Data for midbrain at 2 weeks of age are represented by those for diencephalon since assays were carried out using both tissues unseparated.

Table 3. The selective effect of lead at low dosage on PNMT activities in CNS of rats.

<table>
<thead>
<tr>
<th>2 Weeks of Age</th>
<th>4 Weeks of Age</th>
<th>6 Weeks of Age</th>
<th>8 Weeks of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNMT (+)</td>
<td>TELENCEPHALON</td>
<td>TELENCEPHALON</td>
<td></td>
</tr>
<tr>
<td>Na\textsuperscript{+}/K\textsuperscript{+}-ATPase (-)</td>
<td>PONS / MEDULLA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNMT (+)</td>
<td>DIENCEPHALON</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na\textsuperscript{+}/K\textsuperscript{+}-ATPase (+)</td>
<td>+ MIDBRAIN</td>
<td>TELENCEPHALON</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(+) Indicates change of enzyme activity following lead intoxication compared with control group.

(-) Indicates no changes of enzyme activity following lead intoxication compared with control group.

Table 4. The selective effect of lead at high dosage on PNMT activities in CNS of rats.

<table>
<thead>
<tr>
<th>2 Weeks of Age</th>
<th>4 Weeks of Age</th>
<th>6 Weeks of Age</th>
<th>8 Weeks of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNMT (+)</td>
<td></td>
<td>PONS / MEDULLA</td>
<td></td>
</tr>
<tr>
<td>Na\textsuperscript{+}/K\textsuperscript{+}-ATPase (-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNMT (+)</td>
<td>TELENCEPHALON</td>
<td>DIENCEPHALON</td>
<td>TELENCEPHALON</td>
</tr>
<tr>
<td>Na\textsuperscript{+}/K\textsuperscript{+}-ATPase (+)</td>
<td>PONS / MEDULLA</td>
<td>PONS / MEDULLA</td>
<td>PONS / MEDULLA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(+) Indicates change of enzyme activity following lead intoxication compared with control group.

(-) Indicates no changes of enzyme activity following lead intoxication compared with control group.
result of exposure to lead in this study.

Na\textsuperscript{+}/K\textsuperscript{+}-ATPase is the enzyme which is located in all neural systems. It functions in the active transport of ions across the cytoplasmic membrane. That enzyme localized in the nerve terminal functions in the release and reuptake of neurotransmitters (Godfraind et al., 1975). Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity was increased with age increment in all the brain regions of any groups of rats tested in this experiment. In groups of rats exposed to low or high dose of age-matched control groups and the differences of enzyme activities due to lead intoxication were dose-dependent. These data indicate that the decreased Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity in brain regions is caused by an inhibitory effect of lead on that enzyme. It may be considered that the inhibitory effect of lead on Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity is primarily due to the suppression of either function or development of neural tissue. This interpretation is supported by the report that Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity increases during the period for the formation of dendrites and with an increase in electrical activity of neural tissue (Wu and Phillis, 1981).

PNMT transfers a methyl group from S-adenosyl methionine to the nitrogen of noradrenaline, converting noradrenaline to adrenaline (Axelrod, 1962). It is known to be located in some areas of brain that utilize adrenaline as their neurotransmitter and the adrenal medullary cells for which adrenaline is the primary neurohormone (Saavedra et al., 1974). PNMT is thought to be a marker for adrenaline in the brain (Saavedra et al., 1976). That is to say, it can be considered that the change of activity of PNMT in brain indicates the change of activity of central adrenergic nervous system. In groups of rats exposed to lead, the activity of PNMT was alternative change to that of age-matched control groups. These date indicate that the changes of PNMT activity in brain regions is due to the inhibitory effect of lead on that enzyme. The mechanism of inhibition of activity of PNMT by lead could not be elucidated by the data from the present experiment and further experiments are needed for that purpose.

To test the selectivity of lead toxicity on the nervous system we simultaneously measured and compared the activity changes of Na\textsuperscript{+}/K\textsuperscript{+}-ATPase and PNMT on each brain region. Na\textsuperscript{+}/K\textsuperscript{+}-ATPase is located in all neural tissues and PNMT is located only in central adrenergic nervous system among neural tissues. Therefore, the effect of lead on neural tissue may cause changes of Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity as well as PNMT activity. However, when the effect of lead is selective only on central adrenergic nervous system there may be a change of PNMT activity without concomitant change of Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity.

Thus, selective toxicity of lead to central adrenergic nervous system was determined in the present experiment by comparing Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity and PNMT activity in every brain region of rats employed.

PNMT activity in several regions of brain was changed without concomitant change of Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity following the exposure of animals to lead. In the present experiment, brain regions where PNMT activity was changed without change of Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity were telencephalon andpons/medulla at 2 weeks of age and telencephalon at 4 weeks of age of rats exposed to low dose of lead (Table 3). Those of rats exposed to lead at high dose were pons/medulla at 8 weeks of age (Table 4). It is well known that any tissue can be affected when the dosage of lead is large enough (Bondy, 1986; Costa and Fox, 1983; Fowler et al., 1980; Walsh et al., 1986). Therefore, one possible explanation for these data could be that PNMT in those brain regions might selectively be affected by lead. But it is difficult to reach a concrete interpretation for the mechanism whether selective toxicity was caused by different affinities of lead to these enzymes or by different degree of accumulation of lead in the regions of brain. One explanation for all the remaining regions of brain where Na\textsuperscript{+}/K\textsuperscript{+}-ATPase activity was changed with or without change of PNMT activity following the exposure of animals to lead may be that the effect of lead was not selective on both non-neural and neural tissues including adrenergic nervous system. Another explanation may be that, perhaps, the dosage of lead employed in the present experiment is not low enough to induce differential changes of activities of the two different enzymes.

Since Na\textsuperscript{+}/K\textsuperscript{+}-ATPase is located in all neu-
ral and non-neural tissues of brain and PNMT is uniquely located in adrenergic nervous system, selective effect of lead on PNMT in particular brain regions detected in the present study may be employed as an index representing selective toxicity of lead to central adrenergic nervous system. However, the reason why the selective effect of lead on PNMT is seen inconstantly in terms of regions of brain and ages of animals remains to be further elucidated.

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