

Subclinical Cerebellar Anterior Lobe, Vestibulo-Cerebellar and Spinocerebellar Afferent Effects in Young Female Lead Workers in China: Computerized Posturography with Sway Frequency Analysis and Brainstem Auditory Evoked Potentials

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Abstract: By computerized static posturography with sway frequency analysis, subclinical effects of lead on postural balance was examined in 29 female workers (lead workers) employed at a glass factory for 3–17 (mean 7.9) years in Beijing, China, in relation to brainstem function assessed by brainstem auditory evoked potential (BAEP). Their blood lead concentrations ranged from 26 to 79 (mean 55.7) $\mu\text{g}/\text{dl}$; ages were 21–30 (mean 28) years. Control subjects, aged 22–29 (mean 27.0) years, were 14 healthy female workers at a textile factory located in the same district. With eyes closed, power of the sway of high (2–4 Hz) and low (1 Hz or less) frequencies in lead workers was significantly larger than that in controls; with eyes open, their power of the sway of low frequency was significantly larger ($p < 0.05$). The multiple regression analysis showed that the power of high frequency sway with eyes closed and of low and high frequencies with eyes open were significantly related to blood lead concentrations in lead workers ($p < 0.05$). On the other hand, no significant differences in BAEP latencies between lead workers and controls were observed. The low frequency sway with eyes open was significantly correlated with the high frequency sway with eyes closed in the lead workers. The pattern of changes in postural balance suggested that the anterior cerebellar lobe, vestibulo-cerebellar and spinocerebellar afferent systems were affected asymptotically in female lead workers; the sway of vestibulo-cerebellar and anterior cerebellar lobe types were simultaneously affected by lead. It appears that a computerized static posturography with sway frequency analysis is useful technique for assessment of subclinical lead neurotoxicity.

Key words: Lead, Subclinical effects, Postural balance, Computerized static posturography, Brainstem auditory evoked potential (BAEP)

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Introduction

Subclinical effects of lead on the central and peripheral nervous systems have been widely documented through demonstration of prolongation of latencies in visual, auditory and somatosensory evoked potentials and in event-related potentials¹⁻¹⁴, of impairment of psychological performance^{2, 4, 5, 14-18}, and of slowing of nerve conduction velocities^{1, 4-7, 20-30}.

Some groups of investigators reported that postural balance was adversely affected by lead using a computerized static posturography³¹⁻³⁸. This technique measures displacements of the body's center of pressure in a horizontal plane by the use of a force platform connected to a microcomputer; summary measures generally used were length of the sway path or speed of the sway and the area included within the sway path. Recently, we have introduced the computerized static posturography with frequency analysis of the postural sway into our laboratory³⁹⁻⁴³, as clinical studies had suggested that various disorders which affect cerebellar, vestibular and spinocerebellar-afferent systems are associated with specific types of postural sway, although these associations are still not definite⁴⁴⁻⁴⁹: A lesion of the anterior-cerebellar lobe shows a sway of high frequency (2-4 Hz) predominantly in the anterior-posterior direction with eyes closed; a lesion of the vestibulo-cerebellum (lower vermis) is related to omnidirectional sway of no specific frequencies with eyes open; and a lesion in the spinocerebellar afferent pathway is associated with a sway of low frequency (1 Hz or less), which is omnidirectional but predominantly in the right-left direction with eyes closed.

Thus, using results of the frequency analysis, we observed that the anterior cerebellar lobe, vestibulo-cerebellum and spinocerebellar afferent pathway were adversely affected in lead workers with blood lead (BPb) concentrations of 7-36 (mean 18.0) $\mu\text{g}/100\text{ g}$ and exposure length of 2-34 (mean 14.5) years^{40, 43}. The purpose of the present study is to examine the consistency of our findings on the effects of lead on postural balance system, applying our technique to young female lead workers in China with higher BPb concentrations and shorter exposure length. This would serve information about dose-effect relationships between lead and postural balance, and about its neurotoxicity in females, which have been reported in only few previous studies^{4, 6, 7}.

Brainstem auditory potentials (BAEP) reflect the volume-conducted electric activity from the acoustic nerve, superior olives in the pons, and inferior colliculi in the midbrain, respectively⁵⁰. As it has been demonstrated that the brainstem is involved in postural balance system, the BAEP is measured

in the present study in order to examine if the brainstem function related to the auditory system is also affected by lead.

Subjects and Methods

Subjects

Nature of the procedure in the present study was fully explained to all subjects, and the study was carried out with their informed consent. Subjects examined (lead workers) were 29 female glass workers, aged 21-30 (mean 27.6, SD 2.7) years, who had worked at a glass work factory in Beijing for 3-17 (mean 7.9, SD 3.4) years. Lead was used to color glass; concentrations of lead in air of their workplace were between 0.4 and 1.2 mg/m^3 , according to the report by the manager. BPb concentrations of the workers, measured on blood samples taken just before the postural balance and BAEP study, ranged from 26 to 79 (mean 55.7, SD 13.8) $\mu\text{g}/\text{dl}$. The workers had rarely drunk alcohol and had never smoked. They were not occupationally exposed to local vibration or other chemicals such as cadmium, arsenic, zinc or organic solvents. None of them had ever suffered from neurologic, endocrinological, orthopedic or other confounding disorders, e.g., multiple sclerosis, diabetes mellitus, alcoholic dependency or leg injuries.

Control subjects were composed of 14 female textile workers. These subjects had worked at a spinning industry located in the same district as the glass work factory; their ages ranged from 22 to 29 (mean 25.9, SD 2.5) years. BPb levels in the controls were from 5 to 9 (mean 6.1, SD 1.2) $\mu\text{g}/\text{dl}$, measured as in lead workers. They were not occupationally exposed to neurotoxic substances such as lead or solvents, and had no confounding disorders described above. They also had rarely drunk and never smoked.

Methods

Postural sway: Postural sway was quantitatively measured as described previously by using a strain-gauge-type force platform in a quiet room with flat floor^{6, 7, 39-43}. Subjects were asked to stand quietly on the platform for 60 seconds with eyes open and then for 60 seconds with eyes closed. The right-left and anterior-posterior locations of the body's center of pressure (CP) in the horizontal plane were recorded on a diskette with a sampling interval of 50 μsec using a microcomputer connected to the platform via A-D converter (Analog-Pro, Canopus Electrics Co.). Lengths of the displacement of the CP in the right-left and anterior-posterior directions within each sampling time (a total of 1200 points) were summed up for each direction and defined as the length

of sway path of the CP in the right-left and anterior-posterior directions (i.e., Dx and Dy, respectively). The area included within the sway path during 60 sec (Area) was also calculated.

Displacements of the CP in the both directions were subjected into the Fast Fourier Transformation analysis. The total duration of sampling was 51.2 sec (1024 points). The span of frequencies analyzed was 0.02 to 10 Hz (0.0195 Hz steps). Sum of the root squares of the power calculated from the power spectrum between (1) 0.02 and 0.125 Hz, (2) 0.125 and 0.25 Hz, (3) 0.25 and 0.5 Hz, (4) 0.5 and 1 Hz, (5) 1 and 2 Hz, (6) 2 and 4 Hz, (7) 4 and 8 Hz, and (8) 8 and 10 Hz also served as measures of the amount of postural sway for each frequency range. Using results of the frequency analysis, which of the cerebellar, vestibular and spinocerebellar-afferent systems was affected in the subjects were examined.

BAEP: The measurement of the BAEP was conducted using a four-channel electromyograph (Medelec Sapphire-4ME) by the method described previously in the subjects lying comfortably with their heads supported by a pillow^{4-7, 11, 12, 50}. Click signals (0.1 ms impulses of alternating polarity) were presented to the right ear through earphones at a rate of 20 per second. The intensity of click stimuli was about 80 dB hearing level for each subject. The BAEP was recorded using three standard EEG electrodes fixed to the vertex, right mastoid ipsilateral to stimulation and the left mastoid (ground). The responses were averaged 1024 times after amplification and filtration (bandpass, 200–2000 Hz), with one replication. Peak latencies of the wave I, III and V were recorded, and I-III and III-V interpeak latencies were calculated. The I, III, and V peaks reflect the volume-conducted electric activity from the acoustic nerve, superior olives in the pons, and inferior colliculi in the midbrain, respectively⁵⁰.

Statistical analysis

The significance level of differences in postural balance parameters (Dx, Dy, sum of square root of power spectrum), and BAEP interpeak latencies (I-III, III-V) between the exposed and unexposed workers were tested by Student's t-test. The relationships of postural balance parameters and BAEP latencies to BPb concentration were examined by the simple correlation analysis and by the stepwise multiple regression analysis with postural balance parameters and BAEP latencies as dependent variables and with BPb, age, height and body weight entered and removed as independent variables at $p < 0.05$. All analyses were performed by the SPSS 6.1⁵¹ using a microcomputer.

Results

Differences in postural sway and BAEP latencies between lead workers and controls are shown in Table 1. The Area with eyes closed was significantly larger in lead workers than that in controls. No significant differences were observed in BAEP between the two groups.

Results of the frequency analysis of the sway in lead workers and controls are shown in Table 2. With eyes open, the power of the sway of 0.25–0.5 Hz in the anterior-posterior direction in lead workers was significantly larger than that in controls. With eyes closed, the power of 1–8 Hz sway in the right-left direction and of 0.125–0.25 and 4–8 Hz sway in the anterior-posterior direction was significantly larger in lead workers. Figure 1 illustrates the differences in postural sway between lead workers and controls.

In the multiple regression, the power of the 0.25–0.5 and 1–10 Hz sway in the right-left direction with eyes open and of the 1–4 Hz sway in this direction with eyes closed was significantly related to BPb concentrations in lead workers (Table 3). Figure 2 exemplifies the relationships between postural sway and BPb concentrations in lead workers, showing that the sway of anterior cerebellar lobe type (2–4 Hz with eyes closed) and of vestibulo-cerebellar type (less than 1 Hz with eyes open) was significantly related to body burden of lead.

Correlations between the sway parameters which were significantly increased in lead workers are shown in Table 4 for the workers and controls, respectively.

Discussion

The present study, together with previous ones including us^{7, 31-38, 40, 43}, indicated that lead affects postural balance system in asymptomatic workers. The sway frequency analysis demonstrated that the sway of high frequency (2–4 Hz) was significantly increased and correlated with BPb concentration in lead workers, agreeing the observations among lead workers in our previous study^{40, 43}. This suggests that the sway of anterior cerebellar lobe type is consistently affected in lead workers without clinical lead poisoning. Similarly, the sway of spinocerebellar afferent type, i.e. low frequency (1 Hz or less) sway with eyes closed, is increased in lead workers of the study present here and previous one^{40, 43}, suggesting that this type of sway is also sensitive to subclinical lead effect.

The vestibulo-cerebellar type of sway was adversely affected in the present study as indicated by observations that, with eyes open, the sway of 0.25–0.5 Hz was

Table 1. Differences in postural sway and BAEP latencies between 29 lead workers and 14 control subjects^a

	Lead workers	Controls
Postural sway:		
Eyes open:		
Dx (cm)	41.5 ± 11.9 (20.0–71.4)	36.6 ± 10.2 (23.6–54.5)
Dy (cm)	47.6 ± 12.3 (28.3–73.1)	44.3 ± 12.8 (30.4–79.8)
Area (cm ²)	3.2 ± 1.3 (0.9–6.4)	2.8 ± 1.3 (1.3–5.3)
Eyes closed:		
Dx (cm)	54.1 ± 28.0 (10.3–130.4)	42.2 ± 11.5 (28.4–67.1)
Dy (cm)	59.0 ± 28.8 (7.4–138.3)	50.8 ± 17.4 (24.7–94.5)
Area (cm ²)	3.7 ± 2.0 (0.6–9.9)*	2.4 ± 1.4 (0.9–5.8)*
BAEP latencies:		
I (msec)	1.66 ± 0.09 (1.42–1.84)	1.70 ± 0.15 (1.49–2.08)
I-III (msec)	2.07 ± 0.17 (1.69–2.41)	2.04 ± 0.15 (1.78–2.38)
III-V (msec)	1.78 ± 0.21 (1.56–2.08)	1.75 ± 0.17 (1.56–1.96)

Mean ± standard deviation with range in parenthesis. ^a Abbreviations as in text.
*p<0.05 (t-test).

Table 2. Differences in power spectrum of postural sway (cm) between 29 lead workers and 14 control subjects

Sway frequency (Hz)	Eyes open		Eyes closed	
	Lead workers	Controls	Lead workers	Controls
Right-left direction:				
0.02–0.125	1.20 ± 0.49 (0.52–2.97)	1.17 ± 0.46 (0.50–2.11)	1.05 ± 0.40 (0.30–1.81)	0.85 ± 0.42 (0.43–1.92)
0.125–0.25	0.62 ± 0.21 (0.33–1.14)	0.60 ± 0.27 (0.29–1.34)	0.53 ± 0.18 (0.27–1.18)	0.55 ± 0.22 (0.29–1.02)
0.25–0.5	0.83 ± 0.27 (0.41–1.46)	0.72 ± 0.18 (0.48–0.98)	0.96 ± 0.39 (0.34–2.49)	0.76 ± 0.17 (0.45–0.99)
0.5–1	0.67 ± 0.26 (0.29–1.42)	0.57 ± 0.18 (0.40–1.00)	0.99 ± 0.55 (0.31–2.84)	0.69 ± 0.24 (0.32–1.13)
1–2	0.49 ± 0.19 (0.23–1.14)	0.45 ± 0.14 (0.27–0.71)	0.70 ± 0.38 (0.23–1.76)*	0.48 ± 0.16 (0.29–0.84)*
2–4	0.29 ± 0.13 (0.13–0.75)	0.29 ± 0.10 (0.18–0.53)	0.37 ± 0.23 (0.10–1.16)*	0.26 ± 0.09 (0.16–0.44)*
4–8	0.24 ± 0.12 (0.11–0.51)	0.25 ± 0.10 (0.14–0.52)	0.26 ± 0.14 (0.10–0.61)*	0.18 ± 0.06 (0.12–0.36)*
8–10	0.09 ± 0.05 (0.05–0.20)	0.10 ± 0.04 (0.05–0.20)	0.09 ± 0.05 (0.04–0.23)	0.07 ± 0.03 (0.05–0.15)
Anterior–posterior direction:				
0.02–0.125	0.96 ± 0.25 (0.46–1.72)	0.92 ± 0.31 (0.40–1.52)	0.85 ± 0.29 (0.19–1.35)	0.73 ± 0.26 (0.21–1.00)
0.125–0.25	0.66 ± 0.29 (0.31–1.76)	0.57 ± 0.20 (0.35–1.07)	0.59 ± 0.19 (0.29–1.01)*	0.46 ± 0.17 (0.30–0.84)*
0.25–0.5	0.87 ± 0.25 (0.51–1.43)*	0.71 ± 0.13 (0.54–0.95)*	0.97 ± 0.25 (0.46–1.43)	0.83 ± 0.26 (0.58–1.45)
0.5–1	0.91 ± 0.30 (0.47–1.55)	0.81 ± 0.23 (0.47–1.26)	1.20 ± 0.63 (0.36–3.12)	0.96 ± 0.40 (0.38–1.86)
1–2	0.60 ± 0.19 (0.31–1.01)	0.55 ± 0.22 (0.23–1.16)	0.84 ± 0.35 (0.27–2.21)	0.68 ± 0.26 (0.24–1.16)
2–4	0.28 ± 0.10 (0.13–0.62)	0.30 ± 0.09 (0.10–0.45)	0.36 ± 0.15 (0.11–0.77)	0.30 ± 0.14 (0.12–0.65)
4–8	0.20 ± 0.07 (0.13–0.43)	0.23 ± 0.06 (0.12–0.32)	0.24 ± 0.10 (0.11–0.52)*	0.17 ± 0.05 (0.11–0.27)*
8–10	0.08 ± 0.03 (0.04–0.17)	0.09 ± 0.03 (0.05–0.13)	0.08 ± 0.04 (0.05–0.20)	0.07 ± 0.02 (0.05–0.10)

Mean ± standard deviation with range parenthesis. *p<0.05 (t-test).

significantly increased and of 0.25–0.5 and 1–10 Hz was significantly related to BPb concentration in lead workers. The extent to which this type of sway affected was, however, seems less than that in the previous study⁽⁴⁰⁾ where the sway of a wider range of frequencies (0.125–1 and 2–4 Hz) and Dx and Area of the sway with eyes open were significantly increased in lead workers. BPb concentrations of lead

workers in the present study were higher than those in our previous study (mean 18.0 µg/dl). However, the exposure length of workers was shorter than in the previous one (mean 14.5 years), which might have been resulted in less changes in the vestibulo-cerebellar type of sway.

In the present study, correlation analysis among the sway parameters (Table 4) gave some additional findings: The

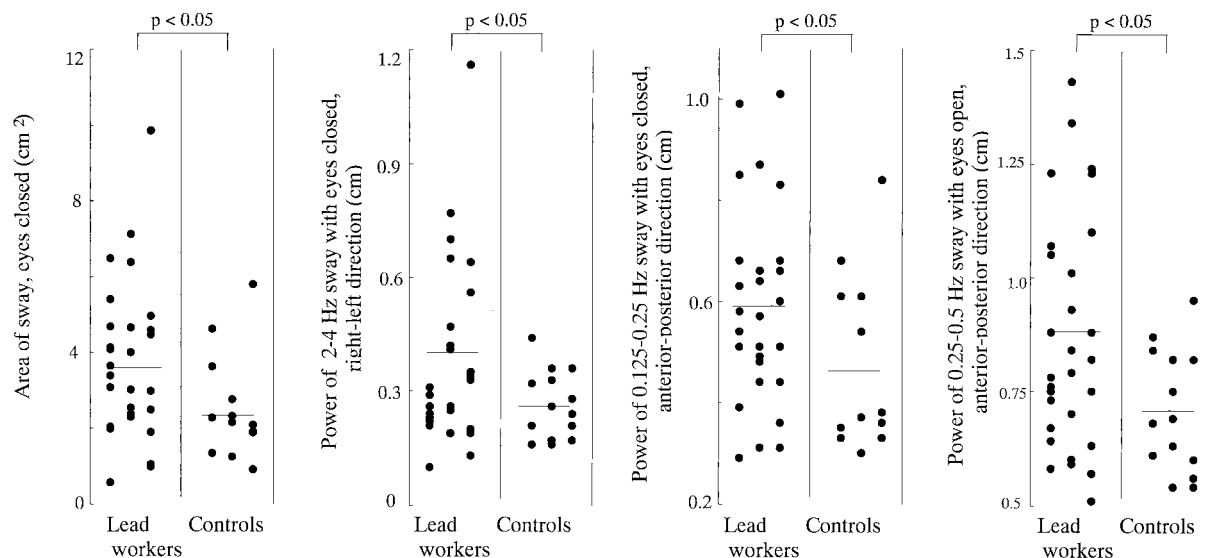


Fig. 1. Differences in postural sway between 29 lead workers and 14 controls.

Table 3. Regressions of postural sway and BAEP latencies (dependent variables) on blood lead (BPb) concentration, age, height and weight (independent variables) in 29 lead workers^{a, b}

Dependent variables	R ^c	Independent variables selected (standardized regression coefficient)
Eyes open:		
right-left		
0.25–0.5 Hz	0.432*	BPb (0.432*)
1–2	0.440*	BPb (0.440*)
2–4	0.513**	BPb (0.513*)
4–8	0.513**	BPb (0.513**)
8–10	0.488**	BPb (0.482**), height (–0.337*)
Eyes closed:		
right-left		
1–2 Hz	0.430*	BPb (0.430*)
2–4	0.390*	BPb (0.389*)

^aThe results are shown only when postural sway or BAEP was significantly related to BPb. ^bAbbreviations as in text. ^cMultiple correlation coefficient.

0.25–0.5 Hz sway with eyes open correlated significantly with the 2–4 Hz sway with eyes closed in the lead workers though this correlation was not significant in the controls. This result may lead to a hypothesis that the sway of vestibulo-cerebellar and anterior cerebellar lobe types are affected simultaneously by lead through a common etiology.

On the other hand, the 0.125–0.5 Hz sway with eyes closed did not correlate significantly with the above parameters in the lead workers or controls. Thus, the lead-induced change in spinocerebellar afferent type of sway could be attributed to a mechanism different from those underlying the alterations

in the remaining two types of sway. As the spinocerebellar afferent type of sway was not significantly correlated with BPb concentrations in the present and previous studies, the dose-effect relationship for the effects in the spinocerebellar afferent pathway still remains to be investigated.

Chia *et al.*^{35, 36} reported that postural sway with eyes closed was much worse than that with eyes open in lead workers whose length of exposure was 0.2–30.5 (mean 7) years and BPb concentrations were 6.4–64.5 (mean 36.0) µg/dl. This seems coincide with the pattern of changes in postural sway in the present study. On the other hand, in our previous

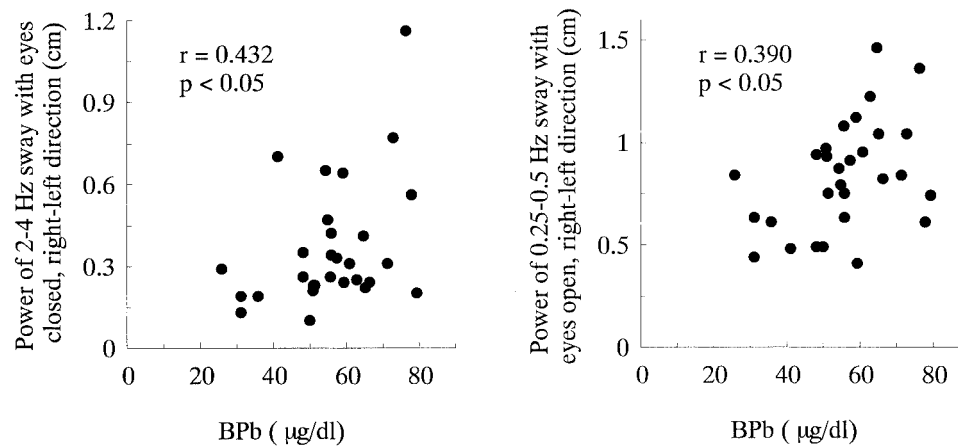


Fig. 2. Relationships between blood lead (BPb) concentration and postural sway in 29 lead workers.
r = Pearson's correlation coefficient.

Table 4. Correlation matrix in postural sway in 29 lead workers (upper trigonal) and 14 controls (lower trigonal)^a

	P1	P2	P3	P4	P5	P6	Area
Eyes open:							
anterior-posterior direction:							
0.25–0.5 Hz (P1)	–	0.587**	0.496**	0.309	–0.197	0.097	0.434*
Eyes closed:							
right-left direction:							
1–2 Hz (P2)	–0.077	–	0.902***	0.674**	0.028	0.213	0.535**
2–4 (P3)	0.021	0.789**	–	0.794***	0.087	0.268	0.523**
4–8 (P4)	–0.051	0.106	0.518**	–	0.034	0.356	0.583**
anterior-posterior direction:							
0.125–0.25 Hz (P5)	0.034	0.592*	0.376	–0.137	–	0.356	0.280
4–8 (P6)	–0.023	0.555*	0.594*	–0.008	0.469	–	0.288
Area	–0.031	0.841***	0.642*	–0.104	0.829***	–0.031	–

^aSway parameters which were significantly increased in lead workers are shown. *p<0.05; **p<0.01; ***p<0.001.

study it was observed that the extent to which the postural sway was affected was greater with eyes open than with eyes closed in lead workers, whose exposure length was longer but concurrent BPb concentrations were lower than those in the two studies as described above. Further studies are necessary to elucidate which part of the nervous system involved in postural balance is sensitive to lead absorption in relation to past exposure.

No significant differences in BAEP latencies were seen between lead workers and controls in the present study. Otto *et al.*¹⁴⁾ reported that prolonged latencies of BAEP waves III and V in children were highly correlated with BPb concentrations of 6–59 µg/dl. The I-III and I-V interpeak latencies of the BAEP were found to be significantly prolonged in children BPb levels of 22.2 ± 8.8 µg/dl, whereas

there were no significant differences in any BAEP interpeak latencies between lead-exposed adults and controls⁹⁾. Hirata and Kosaka⁸⁾ also observed significant prolongation of the III-V interpeak latency in lead workers. On the other hand, some researchers failed to find significant delays in BAEP latencies in lead workers with mean BPb concentrations of 100 µg/dl⁵²⁾ and of 41 µg/dl¹¹⁾. The effects of lead on the auditory nervous system should be further investigated. Also, as technical factors such as click rate and recording bandpass are known to affect results of BAEP measurement⁵³⁾, it should be examined if they underlie the inconsistencies among the previous observations.

In our previous study on the same subjects as presented here, we observed that autonomic nervous system function as measured by the electrocardiographic R-R interval

variability was significantly affected whereas latencies of visual evoked potentials and BAEPs were not significantly changed⁵⁴). It thus remains to be elucidated which part of the nervous system is most sensitive to subclinical lead absorption.

In conclusion, the computerized static posturography with frequency analysis seems useful for assessing the effects of lead on postural balance system at a relatively early stage. Differences in postural sway parameters between the lead workers and controls were not significant, however, when the differences were adjusted for multiple comparison (data not shown). This is probably due to small sample size; a study on larger number of subjects will be necessary to confirm the results presented here.

As discussed in our previous report⁴⁰), it is difficult to explain such functional (subclinical) alterations based on histopathological changes in the nervous system observed in human lead poisoning. Cellular and/or molecular mechanisms underlying the changes observed here should be investigated by further studies. Also, as attention has been paid to prevention of females from the adverse effects of lead⁵⁵), gender differences in the effects of lead on human health should be investigated further. Control for lead exposure should have been necessary in the workplace of subjects examined here, on which we were not able to make a follow-up; preventive measures such as introduction of ventilation system would have been effective as shown in our previous study⁴⁰) that BPb levels decreased substantially in lead workers after enforcement of control of work environment.

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