Cumulative concentrations of blood lead and postural stability

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Abstract

Objective—To study the association in a group of battery manufacturing workers between computerised postural sway parameters and present concentrations of blood lead (PPb), index of cumulative blood lead years (CBI), and cumulative blood lead at different years of exposure (CPbYs).

Methods—Postural stability was investigated with a computerised postural sway measurement system in 60 workers exposed to lead with exposure duration of 84 (range 3–366) months and in 60 control subjects. An index of CBIs in 55 workers (previous blood lead results of five workers were not available) and CPbYs were computed for each worker by calculating the area under the curve of concentrations of blood lead against time.

Results—The mean (SD) PPb was 36.0 (11.7) (range 6.4 to 64.5) $\mu\text{g/dl}$ for the exposed workers and 6.3 (2.4) (range 3.1–10.9) $\mu\text{g/dl}$ for the 14 randomly selected control subjects. Significant differences between groups for the postural sway parameters obtained when the eyes were closed were found for length of sway path (L); mean velocity of the centre of pressure along its path (Vel); area included within the path of the centre of pressure (A_o); 95% confidence elliptical area (A_e). The Romberg ratio (the relation between eyes closed and open) for the Vel, L, A_o , and A_e of the exposed group were also significantly different from those of the controls. The postural sway parameters (eyes closed) were not significantly correlated with PPb or CBI. However, the cumulative blood lead for the past two years before the postural sway assessment, CPbY2, was significantly correlated with all the postural sway parameters.

Conclusion—The study showed that workers exposed to lead had significantly poorer postural stability than a control group. Lead may affect certain parts of the somatosensory system resulting in postural instability when the visual input is cut off. The CPbY2 was significantly positively correlated with most of the postural sway parameters. Effects of lead on postural stability may be related to recent increases in blood lead concentration among the exposed workers rather than to cumulative body burden.

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Postural sway abnormalities have been reported in children with lead intoxication.^{1,2} In adults, there was a case report of possible effects of lead on postural stability by Linz *et al.*³ They reported improvement in postural sway test performance after Ca^{++} EDTA chelation in an adult worker with persistent central nervous system symptoms two years after an episode of subacute lead intoxication.

Recently, we reported that a group of lead battery workers had significantly poorer postural stability than non-exposed workers.⁴ In that study, we were unable to establish a significant relation between present concentrations of blood lead (PPb) and postural sway parameters. This is expected as PPb of the exposed workers were a reflection of present not past exposure. In this present study we examined the association between the computerised postural sway parameters and PPb, cumulative blood lead at different years of exposure (CPbYs), and an index of total cumulative blood lead years (CBI) for each worker exposed to lead.

Material and methods

STUDY POPULATION AND DESIGN

The details of the study population and design have been described in an earlier paper.⁴

The study was carried out at a lead storage battery factory involving 60 workers exposed to lead. None of these workers were chelated before. Sixty subjects, consisting of departmental staff and students, who are clinically healthy and with no exposure to neurotoxic agents served as the control group. Significant differences were noted in the age, height, and blood lead concentrations between the exposed and control groups (table 1). These factors were statistically adjusted in the subsequent analysis. All subjects were found to be clinically normal before they had the postural stability test.

Computerised postural sway assessment

Each subject was given two sets of tests. The first set consisted of three tests (each lasting 20 s) conducted with eyes open. The second set consisted of three tests (also 20 s each) conducted with eyes closed.

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Software supplied by AMTI, BEDAS-2 computer automated stability analysis, was used to compute the parameters relating to the changes in the centre of pressure from data taken while the subject was standing on the platform.

The sway parameters used for detecting changes in performance were: length of sway path (L); mean velocity of the centre of pressure along its path (Vel); area included within the path of the centre of pressure (A_0); and 95% confidence elliptical area (A_e).

BIOLOGICAL MEASUREMENTS

All the exposed subjects and a sample of the controls ($n = 14$) had venous blood collected on the day the postural sway tests were conducted for measurement of whole blood lead concentrations. We did not subject all the controls to a blood test as the history did not suggest any lead exposure. Thus the interviewer randomly approached 14 control subjects to ask if they would volunteer their blood samples. All 14 control subjects agreed. The blood sample was obtained by venepuncture with lead free disposable syringes and was stored in lead free bottles. Blood lead (BPb) was measured with an atomic absorption spectrophotometer with a graphite furnace. External quality control was carried out under the national external quality assessment scheme (NEQAS) in the United Kingdom. The mean coefficients of variation between NEQAS values and our results has been less than 5% for the last 10 years.

Concentrations of BPb had been measured every six months since 1979 for this factory. Past records of BPb were available for 55 out of 60 exposed workers. As an index of the body burden of lead, the cumulative concentrations of BPb for each worker (CPbYe) was computed by calculating the area under the curve of BPb for each year of exposure to lead from the date of the test (postural stability) with the formula:

$$\text{CPbYe} = 0.5 \sum (t_{e+1} - t_e) (\text{BPb}_e + \text{BPb}_{e+1})$$

where t_e = time interval (in years) from the date of the test and BPb_e = blood lead value at the corresponding year (fig 1). Also, CBI—that is, the total blood lead accumulated over the period of working in the factory—was computed for each worker by the same formula with t_e = total years of exposure to lead in the factory. Among the longer serving exposed workers, there were no pre-employment BPb measurements nor regular periodic examinations in the early years. For these

Figure 1 Computation of cumulative BPb for each worker (CPbYe) by years before postural stability test T_e = date of postural stability test; T_0 = time interval (y) from T_e ; BPb_e = blood lead value at the corresponding year.

workers (10 out of 55), the first available BPb reading was linearly extrapolated backwards to a pre-employment value of 6.3 µg/dl. The concentration of 6.3 µg/dl was chosen because this was the mean BPb value of the control group.

STATISTICS

Logarithmic transformation was applied to all the sway parameter data to improve normality. Data for BPb were not log transformed as they were normally distributed. None of the correlation coefficients between the various postural sway parameters and weight, age, and height were more than 0.5. As such, the problem of collinearity was minimised. Differences between the exposed and control subjects' postural sway parameters were tested by analysis of covariance (ANCOVA) with adjustment for age, height, weight, and drinking habits. Education was not taken into consideration as it has never been reported to affect postural stability.⁵⁻⁷ The statistical analysis was run on the IBM 3081 mainframe computer with the Statistical Analysis System (SAS) package. The PROC CORR and PROC GLM procedures were used.

Results

Table 2 shows the adjusted mean postural sway parameters of the exposed and control groups. There were significant differences between them for Vel, L, A_0 , and A_e when the eyes were closed. No significant differences were noted between the exposed and control groups for the sway parameters obtained with eyes open (table 2). The controls' Romberg ratios for Vel, L, A_0 , and A_e were near unity (table 3). There was at least a 20% difference between the values for closed and open eyes of the postural sway parameters (Vel, L, A_0 , and A_e) of the exposed group.

Table 4 shows the Pearson's correlation coefficients (r) between some postural sway parameters (significantly different from the controls) and the different indices of cumulative blood lead. The cumulative blood lead calculated one year before the date of testing is CPbY1. Likewise, CPbY2 to CPbY10 are the values calculated for two to 10 years from the date of postural sway assessment. The postural sway parameters were not significantly correlated with PPb or CBI. The CPbY2 was

Table 1 Characteristics of the study population

	Exposed mean (SD) (n = 60)	Control mean (SD) (n = 60)	P values
Age (y)	31.6 (7.7)	35.4 (7.4)	0.0071
Height (cm)	166.3 (8.1)	169.3 (6.2)	0.0256
Weight (kg)	65.2 (11.7)	64.9 (7.6)	NS
Subjects who drank (%)*	5.0	11.7	NS
Exposure (months)	84.0 (86.7)	—	—
Blood lead (µg/dl)	36.0 (11.7)	6.3 (2.4)†	0.0001

*All of the subjects who drank were occasional and social drinkers, they drank less than once a month, each time no more than two large bottles of beer; †results for 14 control subjects.

Table 2 Postural sway parameters for exposed and control groups

Eyes condition	Postural sway parameters	Exposed* mean (SE) (n = 60)	Control* mean (SE) (n = 60)	P values
Open	Vel (cm s ⁻¹)	0.77 (0.09)	0.74 (0.09)	NS
	L (cm)	15.40 (0.09)	14.70 (0.09)	NS
	A _o (cm)	1.67 (0.16)	1.51 (0.17)	NS
	A _e (cm)	0.84 (0.19)	0.76 (0.19)	NS
Closed	Vel (cm s ⁻¹)	0.93 (0.09)	0.77 (0.09)	0.0014
	L (cm)	18.50 (0.09)	15.40 (0.09)	0.0014
	A _o (cm)	2.25 (0.16)	1.55 (0.16)	0.0002
	A _e (cm)	1.03 (0.17)	0.74 (0.17)	0.0018

*Geometric mean value adjusted for height, weight, age, and drinking habits. SE = standard error on a log scale.

Table 3 Romberg ratios (RRs) for some postural sway parameters between the exposed and control populations

Postural sway parameters	Exposed RR* (n = 60)	Control RR* (n = 60)	P values
Vel	1.20	1.04	0.0206
L	1.20	1.04	0.0207
A _o	1.34	1.02	0.0100
A _e	1.23	0.98	0.0311

*Romberg ratio (RR) = ratio of the postural sway parameters measured with eyes closed and eyes open.

significantly correlated with all the postural sway parameters. Also, CPbY9 was significantly correlated with the postural sway parameters A_o and A_e. Table 5 was tabulated to examine if the significant association found earlier between CPbY2 and most of the postural sway parameters could have been contributed by workers with longer exposure. Table 5 shows the *r* values between the postural sway parameters and the different CBIs for workers excluding the 22 workers with more than six years of exposure who have contributed to CPbY9 (table 4). The *r* values for CPbY2 with the postural parameters were, in fact, stronger showing that the observed association was not affected by the group of workers with longer exposure (table 5).

Table 4 Pearson's correlation coefficients between various postural sway parameters and different indices of cumulative blood lead concentration by years for all workers

	Exposed postural sway parameter (eyes closed)			
	Vel	L	A _o	A _e
PPb (n = 60)	0.129	0.129	0.238	0.233
CBI (n = 55)	0.071	0.070	0.094	0.110
CPbY1 (n = 55)	0.066	0.066	0.127	0.122
CPbY2 (n = 45)	0.343*	0.343*	0.405**	0.367*
CPbY3 (n = 41)	0.111	0.111	0.110	0.080
CPbY4 (n = 36)	0.121	0.121	0.182	0.204
CPbY5 (n = 31)	0.207	0.206	0.232	0.233
CPbY6 (n = 27)	0.073	0.072	0.193	0.239
CPbY7 (n = 25)	-0.019	-0.020	0.156	0.241
CPbY8 (n = 23)	-0.121	-0.121	0.094	0.222
CPbY9 (n = 22)	0.271	0.270	0.431*	0.443*
CPbY10 (n = 19)	0.132	0.131	0.304	0.369

*P < 0.05; **P < 0.01.

Table 5 Pearson's correlation coefficients between various postural sway parameters and different indices of cumulative blood lead concentration by years for all workers with ≤ 6 years of exposures

	Exposed postural sway parameter (eyes closed)			
	Vel	L	A _o	A _e
PPb (n = 38)	0.129	0.198	0.285	0.257
CBI (n = 33)	0.162	0.162	0.204	0.169
CPbY1 (n = 33)	0.131	0.131	0.162	0.122
CPbY2 (n = 23)	0.630**	0.630**	0.599**	0.485*
CPbY3 (n = 19)	0.431	0.431	0.189	-0.046
CPbY4 (n = 14)	0.480	0.480	0.406	0.251
CPbY5 (n = 9)	0.663	0.664	0.506	0.276
CPbY6 (n = 5)	0.559	0.559	0.541	0.388

*P < 0.05; **P < 0.01.

Figure 2 Mean (95% CI) concentration of blood lead for workers with more than six years of exposure.

Figure 3 Mean (95% CI) concentration of blood lead for workers with less than six years of exposure.

Figure 2 shows the mean (95% confidence interval (95% CI)) blood lead concentration by year of examination from 1983 until 1993 (the year of the postural sway assessment) for exposed workers with more than six years of exposure. Although data were available from 1979 to 1982, these only apply to a few workers (< 10) and thus were not represented in the figure. Since 1983, the mean BPbs for the factory have been declining; with a plateau from 1985 to 1988. However, there was an increase in the mean BPb from 1989 until 1991, declining in 1992 and 1993 (year of the postural stability assessment). There was a gradual increase in the mean BPb of the workers with ≤ six years of exposure from 1987 to 1989 (fig 3). The mean BPb was fairly constant from 1989 to 1991, with a decline again from 1992 to 1993.

Discussion

To our knowledge, our earlier study is the only report of postural instability among a group of workers exposed to lead compared with non-exposed workers. In that study, we were unable to establish a significant relation between present blood lead concentrations and postural sway parameters. Present blood lead concentrations of the exposed workers were primarily a reflection of exposure received in the most recent few months (not past exposure), especially in currently exposed workers.⁸ The action of lead on the nervous system would require time to exert and manifest its effects. In this paper, we showed that there was a significant association between most of the postural sway parameters and the cumulative blood lead in the previous two years from the date of the postural assessment (tables 4 and 5). Present blood lead concentrations were poorly correlated with most of

the postural sway parameters (table 4). Given the present blood lead concentrations, it would be unrealistic to expect an acute effect of lead on the nervous system and thus an effect on postural stability. Therefore, the poor correlation of present concentrations of blood lead with postural sway parameters is understandable.

It was expected that the index of cumulative blood lead would be associated with the postural sway parameters. This was not our finding. The lack of relations between the index of cumulative blood lead and various postural sway parameters could be due to our present method of measurement of the index which may result in an underestimation of the worker's actual cumulative blood lead. We have adopted a pre-employment blood lead of $6.3 \mu\text{g/dl}$ for the 10 workers who do not have a baseline value. As such, their index of cumulative blood lead would be extrapolated based on $6.3 \mu\text{g/dl}$. The workers' baseline blood lead may be higher than $6.3 \mu\text{g/dl}$, especially in the early 1980s. Phoon and Ong⁹ reported mean blood lead concentrations of $16.4 \mu\text{g/dl}$ among sedentary workers with no known direct exposure to lead. If $6.3 \mu\text{g/dl}$ is an underestimation of the workers' baseline lead, the underestimation would increase with an increasing time interval between date of joining and date of first lead measurement. However, as pointed by Phoon and Ong: "... observations mentioned in this paper are not representative of all worksites in Singapore."⁹ In the absence of the general population data on baseline lead, we thought it would be more appropriate to base our extrapolation on the concentrations of blood lead in controls.

On the other hand, the lack of relations between index of cumulative blood lead and various postural sway parameters suggests that the effects of lead on postural stability may be reversible and therefore not associated with the index of total cumulative blood. As shown in the results, the Pearson's correlation coefficients for CPbY2 with Vel, L, A_o, and A_c range from 0.34 to 0.41 when all the workers were considered (table 4). However, the correlation coefficients for CPbY2 with Vel, L, A_o, and A_c (table 5) all showed increases (ranges from 0.49 to 0.63 with accompanying increase in significance in spite of the smaller sample size) when all the workers with more than six years of exposure were removed from the analysis.

Linz *et al*⁵ reported an improvement in postural sway test performance after Ca⁺⁺ EDTA chelation in an adult worker with persistent central nervous system symptoms two years after an episode of subacute lead intoxication. The patient was a 37 year old construction carpenter who two years previously, before being seen by the authors, had been working for several months cutting steel to dismantle a bridge. His blood lead concentrations went from a baseline of $15 \mu\text{g/dl}$ to $109 \mu\text{g/dl}$ and he was removed from the job. A platform posturography was performed on the worker with a computerised force platform. Three trial mean scores and the composite score were below the normal range for three of six subtests evaluating

sensory organisation. The worker was chelated with intravenous Ca⁺⁺ EDTA for five consecutive days. Five days after the infusion, the platform posturography showed improved sensory organisation over prechelation findings. Only one of six subtests of sensory organisation was marginally abnormal. Although none of our workers exposed to lead were chelated, there were periods in their employment history, especially from 1992 onwards (figs 2 and 3), when their exposures to lead were lower. This may have provided the opportunity for recovery.

The cumulative blood lead for the past two years before the postural sway assessment, CPbY2, was significantly correlated with all the postural sway parameters. This suggests that an increase in postural instability may be related to an earlier increase in the blood lead concentration. From 1988 until 1991, the mean blood lead concentrations of the workers were above $40 \mu\text{g/dl}$. It was only from 1991, two years from the date of the postural test, that the mean blood lead concentrations had declined (fig 3). Could the higher blood lead then have affected the nervous system resulting in some postural instability?

The posture of a person depends on the degree and distribution of muscle tone and, therefore, on the activity of the motor neurons that supply the muscles. The motor neurons in the anterior grey columns of the spinal cord are the convergence points for the nervous impulses from many posterior nerve roots and the descending fibres from many different levels of the brain and spinal cord.¹⁰ Postural stability is affected by sensory information from the vestibular, proprioceptive, and visual system with the cerebellum as the centre that controls the information.^{11 12}

Nerve dysfunction involving mainly peripheral nerves has been reported to occur with blood lead as low as $40 \mu\text{g/dl}$.^{13 14} Jeyaratnam *et al*, in a study of 46 workers exposed to lead, reported significantly prolonged somatosensory evoked potentials of the posterior tibial nerves among exposed workers with a mean blood lead concentration of $48.7 \mu\text{g/dl}$.¹⁵ The somatosensory evoked potential assesses the whole sensory neural axis inclusive of the proximal parts of the peripheral sensory nervous system (root and plexus). The somatosensory system continually provides the central nervous system with information about the position and rate of change in position of the body and its parts. The spinal cord, brain stem reticular formation, and cerebellum all use this afferent information to constantly readjust muscle tone.¹⁶ Lead may have affected the somatosensory system of the exposed workers resulting in the poorer postural stability compared with the controls.

Bhattacharya *et al* have reported postural instability among children who were exposed to lead.¹² In a cohort of 33 children (mean blood lead of $23.5 \mu\text{g/dl}$), Bhattacharya *et al*¹ reported that the maximum blood lead incurred during the second year of life was significantly positively related to postural sway (area of sway). In a later study, involving 63

children, the results showed a significant relation between postnatal blood lead concentration and postural balance.² However, in both the studies the mechanism of the postural instability among the children was not discussed.

In summary, the study showed that workers exposed to lead had significantly poorer postural stability than a control group. Lead may affect certain parts of the somatosensory system resulting in postural instability when the visual input is cut off. The cumulative blood lead for the two years before the postural sway assessment, CPbY2, was significantly positively correlated with most of the postural sway parameters. Effects of lead on postural stability may be related to recent increases in concentrations of blood lead among the exposed workers rather than cumulative body burden.

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