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The Relationship between Children's Blood Lead Level and Postural Stability

by

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Children, especially younger, are recognized as very susceptible to environmental lead exposure. In order to assess the effect of lead on spontaneous postural sway, we studied 327 children 4-13 years old, living in 4 cities in Upper Silesia an industrial region of Poland. Lead concentration in blood was measured by absorption atomic spectrometry (AAS) and posturography was performed using CATSYS 2000 - SWAY 7.0 equipment. Children's postural sway characteristics decreased with age. Particular variables had higher values for boys than girls and were positively associated with blood lead levels. There was an association between postural sway characteristics and smoking habits of mother, usage of aminoglycosides and paracetamol. Posturography seems to be a useful tool for assessment of lead exposure effects on the nervous system at low blood lead levels.

Keywords: environmental exposure to lead, children, postural stability

Introduction

Lead is the most studied metal and knowledge about adverse health effects of lead, especially of its high concentration, are well known. Studies on the effects of lead in children have demonstrated a relationship between exposure to lead and a variety of adverse health effects. Central and peripheral nervous systems are targets of lead (see: review of effects in ATSDR Toxicological profile for Lead, 2007). The side effects also include impaired mental and physical development, decreased heme biosynthesis, elevated hearing threshold, and decreased serum levels of vitamin D.

Majority of the studies on human exposure to lead, and the health effects of it, are based on B-Pb data. The clinical manifestations of lead toxicity are called plumbism and a summary of

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symptoms associated with B-Pb is shown in table 1.

Majority of studies on environmental exposure to lead have been focused on the behavioral and cognitive effects in children exposed to lead, less interest has been focused on neurological impairment induced by low lead levels. There is no doubt that lead exposure cause's decrease in children IQ, poor school performance, problems with control of emotions and attention deficits. (Schwartz, 1994; Winneke and Krämer 1997, Lanphear et al 2005). Winneke & Krämer (1997) established that doubling B-Pb form 10 to 20 μg/dL is associated with an average loss of 1-3 points of IQ. Lanphear et al (2000) showed that cognitive deficits were associated with B-Pb concentration below 5 ųg/dL. Chioto et al (2004) showed neurobehavioral deficits in relation to low levels of lead in the areas of intelligence, reaction time, visual-motor integration, fine motor skills, attention, including executive function, off-task behaviors, and teacher-reported withdrawn behaviors.

There are two studies reporting that elevated B-Pb levels correlated with EEGs recordings characterized as: abnormal ($R=0.419$; $p<0.001$), border-line ($R=0.206$; $p<0.005$), epileptiform ($R=0.282$; $p<0.01$) and focal ($R=0.256$; $p<0.05$). Spectral analysis of brain activity evidenced increased theta band power ($R=0,229$, $p<0,05$) both in Poblano et al. (2001) and Pawlas et al (2002) studies.

Several studies showed associations between lead exposure and auditory function in children. Increasing of hearing threshold with blood lead level has been found in studies of Robinson et al (1985), Schwartz and Otto (1991), Osman et al (1999). Some papers showed effects of environmental lead exposure on hearing and posture. Otto et al (1985) revealed an increase in latencies of waves III and V of the brain auditory evoked potentials (BAEPs) associated with B-Pb measured 5 years prior to the tests (mean, 28 μg/dL). Recent research has shown that I–V and III–V interpeak intervals decreased as B-Pb increased from 1 to 8 μg/dL and then increased as B-Pb rose from 8 to 31 μg/dL. Osman et al (1999) reported increased latency of wave I of the BAEP in children with B-Pb above 10 μg/dL compared to children with B-Pb below 4.6 μg/dL. Rothenberg et al. (2000) hypothesised that the negative linear term was related to lead effect on brainstem auditory pathway length, and that the positive term was related to neurotoxic lead effect on synaptic transmission or conduction velocity. The auditory and vestibular systems are intimately connected anatomically. So impairments of auditory system may be associated with impairment of vestibular system which contributes to maintaining balance. Indeed, Bhattacharya et al (1990) have found that the ability to maintain upright postural balance in children is significantly associated with blood lead level. Similar results have been shown by others (Dietrich et al, 1992; Despres et al, 2005; Fraser et al, 2006; and Batthacharya et al, 1995, 2006, 2007).

The central nervous system which contributes to cognitive development also plays a significant role in neuromotor functioning of human, especially young children. Maintenance of upright posture is processed by the brain and depends on inputs from visual, proprioceptive and vestibular receptors. So, stability of upright position requires an interaction of peripheral and central nervous system, and may be affected by neurotoxicants. Postural stability seems to be a good tool for examining the early effects of toxins on the nervous system. The purpose of the present study was to assess if children's posture stability is affected by exposure to lead.

Material and methods

The study has been carried out with the approval of the Ethics Committee of the Institute of Occupational Medicine and Environmental Health in Sosnowiec (IMPiZŚ 7/1999), according to the Helsinki protocol. The informed consents were obtained from all tested subjects.

The study group consisted of 327 children (183 boys and 144 girls) 4-13 years old, living in 4 cities in Upper Silesia Region of Poland, (all located in the vicinities of lead plants).

Examined protocols included medical questionnaire, otorhinolaryngological examination, audiometric measurements, posturography and blood sampling. Audiometric measurements consisted of tympanometry with impedance audiometry (Madsen, model Zodiac 901).

Table 1

Exposure to lead heath effects of in children and adults in dependence on lead concentration in blood (B-Pb)

Symptom	Blood lead level in mg /dL	
	children	adults
death	125	150
kidney and brain damage	80 - 100	100 - 120
frank anaemia	40-70	50-80
colic	60	
reduction of haemoglobin synthesis	25 – 30	50
elevation of urinary ALA and coproporphyrine	40	
increase of systolic blood pressure		30
slowed nerve conduction in peripheral nerves	20	30-40
increase of protoporphyrine in erythrocytes	15	20 - 30 men 15-20 women
reduction of vitamin D_3	10 - 15	
inhibition of ALAD	>10	>10
developmental toxicity	10	
hearing acuity	<10*	30
decrease of IQ and growth retardation	<10*	>50

Blood was taken by venipuncture from the anticubital vein into test tubes containing sodium heparin (Vacutainer, Becton Dickinson International, USA). Lead in blood samples were measured by absorption atomic spectrometry (AAS) using the Perkin-Elmer 4100ZL instrument. Posturography was performed using CATSYS 2000 - SWAY 7.0 (Danish Product Development Ltd.). The Sway System is a platform containing three orthogonal strain–gauge devices. The Sway System is a force platform containing three orthogonal strain–gauge devices. The devices record movements of the force center in the XY-plane surface and provide information such as RMS sway, sway velocity, sway area, antero-posterior and lateral sway, and known from literature (e.g. Polechoński and Błaszczyk, 2006). The platform was linked to a PC via data logger so, sway parameters has been calculated on-line by the software and final results were displayed on a screen and recorded on the disk. Parameters calculated by the software included: mean sway (defined as the simple mean of the distance from the geometrical mean force center position to all recorded force center positions during the test), sway area (SA; defined as the area of the smallest polygon, which includes the total trajectory of the force center in the horizontal force plate plane), sway velocity (SV; calculated by dividing the total length of the force center trajectory in mm with the recording period length), sway index (SI; defined by manufacturer, this variable not used in this study), displacement in lateral direction (SAGIT) and displacement in anterior - posterior direction (Transversal). The Transversal sway and the Sagittal sway are defined as the simple mean of the recorded x and y values of the force center in a coordinate system with the mean force center position.

The examination procedure was similar to that used by Bhattacharya at the University in Cincinnati (Bhattacharya and Linz, 1991). Sway of the body was recorded under four conditions, while standing on the platform, each lasting 30 seconds, with eyes opened (EO[1]). During this test condition, all receptors contribute to maintaining body upright position with no modification and sway is smallest.

- eyes closed (EC), - signals from vision are switched off, and response reflects the availability of cues from proprioreceptors and slightly increased input from vestibular system in comparison to EO condition, sway area is larger than in previous testing conditions, and depends on signals processing by central nervous system (CNS)

[1] *(EO) – eyes open, (EC) – eyes closed (ECF)- eyes closed on foam, (EOF) -eyes open on foam, (EOnF) - eyes open non foam, (ECnF) -eyes closed non foam*

Table 2

Demographic data of children.

	all			Boys			Girls		
	Average	Min.	Max.	Average	Min.	Max.	Average	Min.	Max.
Number of subjects	327			183			144		
Age (years)	6,6 ±1,37	3.0	12.0	6,8 ± 1.46	4.0	12.0	6,5 ± 1,23	3.0	11.0
High (cm)	122,0 ± 8,37	100.0	154.0	122,7 ± 8,9	105	150.0	121,3 ± 7,65	100.0	154.0
Body mass (kg)	23,5 ± 5,33	14,5	49.0	24,4 ± 6.1	14,5	49.0	22,5 ± 4,02	15.0	36.0
Hearing treshold	6 right	-7	45	6	-5	45	6,5	-7	39
(dB HL)	5 left	-8	78	5	-8	78	5	-6	36
Average blood lead level (µg/L)	63,9 ±41,5	22	230	69,5 ±46	23	230	57,3 ±34,4	23	196
Average sway area (mm^2)	(EO) 222 ±171,5	9	1246	236 ±144	9	881	207 ±198	38	1246
	(EC) 377 ±320	48	2620	406 ±288	57	1708	342 ±351	48	2620
	(EOF) 267 ±197	44	1403	281 ±181	61	1099	250 ±214	44	1403
	(ECnF)460 ±319	64	2443	497 ±326	64	2443	414 ±305	68	1955

- eyes opened and foam pad under feet (EOF),- reflects the presence of visual control, aberrated signals from proprioreceptors and slightly increased input from vestibular system in comparison to EO condition, and depends on how CNS is able to process changed signals
- eyes closed and foam pad under feet (ECF) – there is no visual input, and input from proprioreceptors is incorrect, so this condition requires higher reliance on vestibular system and CNS in comparison to other test conditions.

The subjects were asked to stand without shoes directly on the platform, as still as possible with eyes fixed on a point located before them at the level of their eyes. Data obtained from investigated subjects became a source of following parameters: Sway Area (SA), Sway Velocity (SV), antero-posterior sway (Trans), and lateral sway (Sagitt). Following Bhattacharya, special ratios have been calculated. These ratios reflect:

- the effect of change in vision (vision ratio=EC/EO),
- the sole effect of change in proprioreception (Proprioreception ratio=EOF/EOnF) and
- the effect of highest reliance on vestibular system (Vesitibular ratio= ECF/ EOnF).

Hearing examination was supplementary to the study of posture. It provided information about middle ear status and allowed to assess hearing threshold. Any inflammatory process in middle ear might affect vestibular system.

The examination was performed on the blind basis. Statistical analysis of results was carried out using appropriate procedures. Mann–Whitney U-test was used to compare differences between boys and girls in blood concentrations of elements. Spearman rank correlation analysis was performed to evaluate possible associations between concentrations of lead and different variables from the questionnaires as well as associations between the sway parameters. Multivariate analysis was applied in order to estimate the association between levels of sway parameters and their potential determinants. The level of statistical significance was set at $p<0.05$.

Table 3

Multivariat regression analysis forward step procedure.

Dependent variable	Independent variable	B	SE B	p- value	R^2	p
SA- EO	intercept	550,52	141,00	0,00	0,25	0.003
	age	-91,59	23,11	0,00		
	lead	1,47	0,77	0,06		
	aminoglycosides	106,10	59,33	0,08		
	body mass	6,05	4,19	0,15		
	gender	51,94	36,23	0,16		
SV-EO	intercept	18,91	3,05	0,00	0.19	0.011
	age	-1,57	0,51	0,00		
	aminoglycosides	2,47	1,39	0,08		
	gender	1,29	0,85	0,13		
	lead	0,02	0,02	0,23		
SA-EC	intercept	853,89	279,80	0,00	0.16	0.049
	aminoglycosides	265,80	128,87	0,04		
	age	-95,76	46,88	0,05		
	mother's smoking	-91,05	78,26	0,25		
	paracetamol	105,30	91,65	0,26		
	lead	1,63	1,61	0,32		
SV-EC	intercept	22,94	4,35	0,00	0,12	0,041
	age	-1,75	0,73	0,02		
	lead	0,05	0,03	0,07		
	gender	22,94	4,35	0,15		
SA – EOF	intercept	346,04	121,19	0,01	0,25	0,006
	age	-59,19	18,88	0,00		
	mother's smoking mother	63,65	31,56	0,05		
	gender	57,79	29,99	0,06		
	lead	1,12	0,63	0,08		
	paracetamol	63,91	35,77	0,08		
	body mass	6,06	3,52	0,09		
SV-EOF	intercept	16,81	2,56	0,00	0,21	0.005
	age	-1,15	0,42	0,01		
	gender	1,49	0,70	0,04		
	mother's smoking	1,43	0,74	0,06		
	lead	0,02	0,01	0,31		
SA-ECF	intercept	591,42	191,61	0,00	0,17	0.018
	age	-99,69	31,93	0,00		
	lead	2,91	1,04	0,01		
	Body mass	11,83	5,95	0,05		
	mother's smoking	57,46	51,74	0,27		

Results

From 700 children invited to the study parents of 327 ones responded. The study group consisted of 327 children, aged 3-12 years with average lead concentration in blood: 63,9 ± 41,5 µg/L. Blood lead levels ranged from 22 µg/L to 230 µg/L. Demographic data are shown in table 2.

Table 3 continue

Dependent variable	Independent variable	B	SE B	p- value	R^2	p
SV-ECF	intercept	6,35	9,03	0,48	0,24	0.004
	age	-2,72	0,72	0,00		
	lead	0,06	0,02	0,01		
	high	0,19	0,08	0,02		
	mother's smoking	2,39	1,16	0,04		
	gender	1,87	1,12	0,10		
Trans -EOF	Intercept	6,05	1,23	0,00	0,24	0,004
	age	-0,58	0,21	0,01		
	lead	0,01	0,01	0,05		
	paracetamol	0,71	0,39	0,07		
	mother's smoking	0,92	0,49	0,07		
Trans- ECF	intercept	3,55	1,19	0,01	0,12	0,084
	lead	0,02	0,01	0,02		
	gender	0,48	0,31	0,13		
	age	-0,28	0,20	0,16		
	body mass	0,04	0,04	0,29		
Sagi ECF	intercept	8,50	1,36	0,00	0,09	0,047
	age	-0,45	0,21	0,03		
	paracetamol	-0,66	0,45	0,14		

There were no significant differences in demographic data between boys and girls. The examined group was split into two subgroups depending on blood lead level: (1) - 258 children with B-Pb up to 10 μg/L according to current CDC (Center for Disease Control, USA) recommendation for lead and (2) - 50 children with B-Pb above 100 μg/L. Parents of 58 children did not agree for blood sampling. Figures 2 to 6 present changes of body sway parameters consecutively: SA, SV, Trans, Sagitt and above described body sway ratios for sway area only. As seen on figures 2-5, examined group was split into 3 subgroups: (1) children with BPb up to 30 μg/L, (2) children with B-Pb 31-60 μg/L and (3) children with B-Pb above 60 μg/L. The sway variables are increasing with blood lead levels, however variable Transversal for ECF test conditions as well as variable Sagittal in ECnF conditions the middle group in comparison to group with highest BPb were higher or lower, respectively. Sway velocity and sway area increased statistically significantly in the group with B-Pb>100 μg/L in absence of visual input. The same was observed when children stood on the foam pad and proprioreceptors gave incorrect cues. Sway parameters reached the highest values in subjects from both subgroups tested with eyes closed and during standing on foam pad, especially in children with B-Pb > 100 μg/L. Figure 6 shows sway ratios for two subgroups: one- with blood lead levels below 100 μg/L and second - above 100 μg/L. Subgroup with lower BPb may be referred to as control. The cut-off equal 100 μg/L is based on current recommendation of CDC as well as current Polish recommendation for treatment.

Spearman rank correlation analysis showed that body sway decreases with age, variables have higher values for boys than girls and are positively associated with blood lead levels. No statistically significant relationships were found between sway parameters and both body length and weight of children. There was an association between body sway and smoking habits of mother, usage of aminoglycosides and paracetamol. There was no correlation with neurological health history on the basis of questionnaire; however the history of head trauma made some of the studied parameters significantly worse. Age was positively correlated with blood lead levels in the examined group. Age is a confounder, hence multivariate statistical analysis were used to adjust result for

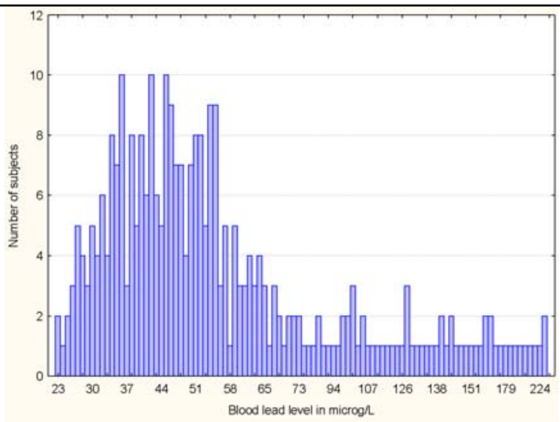

Figure 1
Distribution of blood lead levels in examined children

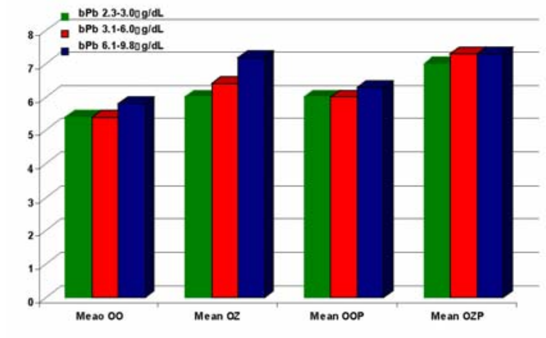

Figure 2
Posturography results in relation to blood lead concentration – parameter MEAN.

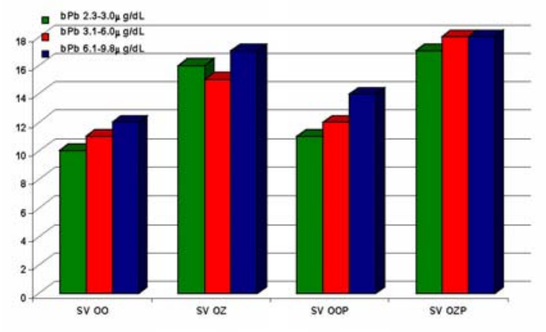

Figure 3
Posturography results in relation to blood lead concentration – parameter SA

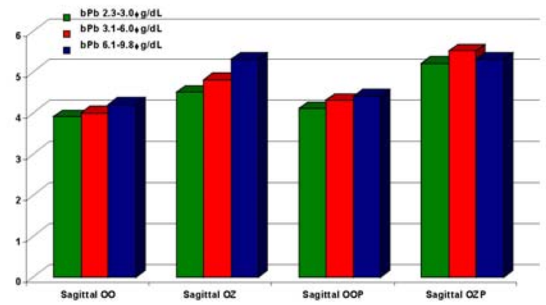

Figure 4
Posturography results in relation to blood lead concentration – parameter Sagittal

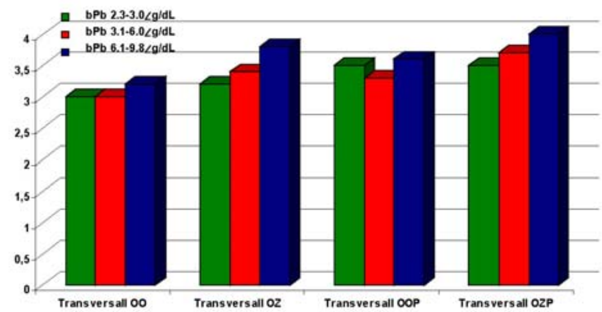

Figure 5
Posturography results in relation to blood lead concentration – parameter Transversall

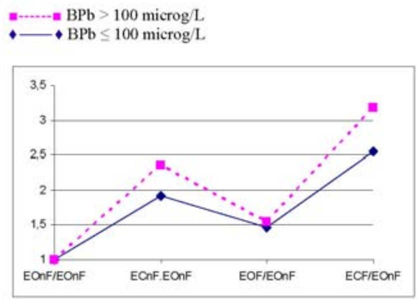

Figure 6
Sway ratios calculated for sway area

this factor. No control group is appropriate due to common environmental exposure to lead.

Summary of multi variables regression analysis with the forward step procedure is shown in table 3. Only statistically significant results are included. Although body sway examination was performed for 241 subjects, due to missing data results obtained from only 67 subjects were calculated by multivariate analysis.

Discussion

Body sway has many parameters which are not completely independent, e.g. sway area is linked to increasing sway velocity, sway displacement in both sagittal and transversal directions. Pearson correlation coefficients (range from 0.63 to 0.90, $p<0.05$) between every parameters of body sway were found. Body sway area and (Romberg-like) sway ratios values are the most frequently considered parameters of body sway in literature (Depres et al, 2005, Bhattacharya et al, 1990, Raymarkers et al, 2005). These parameters were chosen in the mentioned papers for the assessment of lead effect on body sway; however, force centre positions might be assessed in different way, and it is difficult to compare directly results reported in literature.

Trends in changes in sway parameters observed in this study are similar to those reported by Bhattacharya (1995), however they obtained their results at higher blood lead concentrations when it is easier to get overt effects. Different test conditions resulted in different outcomes. Each testing condition when eyes were closed gave worse results compared to appropriate conditions with eyes open. Eyes closed conditions require more intense engagement of higher levels of the nervous system to maintain upright position of the body, especially when subject is standing on foam. Sway area increased with blood lead elevation, even at low concentration, so it could indicate that the nervous system is influenced even at low blood lead levels.

Large inter-subject variability was found, so the size of the group seems to be too small to get pronounced results. Many studies reported recently that variability in susceptibility to lead exposure as well as variability in health outcomes is thought to be modified by genetic polymorphisms of ALAD gene, vitamin D receptor (VDR) gene and hemochromatosis gene (Hu et al, 2001; Bellinger et al, 1994; Bergdahl et al, 1997; Sakai 2000; Skerfving 2005). Polymorphisms of these genes are associated with lead metabolism, and may explain varied susceptibility to lead. In case of some genotypes, exposure to lead may develop more serious health effects. Chakraborty et al (2008) studied the effect of lead exposure on neuromuscular response of children in dependence of other polymorphism. They studied polymorphism of VDR, dopamine receptors (DRD2 and 3), and N-acetyltranferase-2 (NAT2) and they reported that children with certain specific genotypes showed enhanced detrimental effects of lead exposure on neuromuscular function, even below 100μg/L. They concluded that for such children blood lead level exceeding 88μg/L was already neurotoxic. This may explain, at least partially, great variability observed in our study. Obviously, it is only a suggestion, because genotyping was not available for this study.

Age was a strong confounder in this study and was negatively associated with sway parameters, contrary to blood lead level. It may reflect the maturation of the peripheral nervous system.

Conclusions

This study demonstrates that effects of lead, observed even at low concentration in blood, varied largely between subjects, as it was expected. Body posture is affected by lead, and body sway increases with elevation of BPb. Posturography seems to be a useful tool for the assessment of low level lead exposure effects on the nervous system at low blood lead levels.

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