Hair Lead and Cadmium Levels and Specific Depressive and Anxiety-Related Symptomology in Children

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Abstract

This study investigates the relationship between hair lead and cadmium levels and specific, sub-clinical emotional problems in a sample of urban children. Information about the presence of the depressive and anxiety-related symptomatology considered was derived from parental responses to the Walker Problem Behaviour Identification Checklist. Chi-square analyses and logistic regression analyses were used in order to assess the relationship between lead and cadmium exposure status (as ascertained through hair elemental analysis) and the presence or absence of each behavioural descriptor considered. The results obtained suggest that lead exposure is significantly associated with anxiety-related behavioural symptomatology, both before and after controlling for the effects of social and family status, subject age, and subject sex.

Introduction

Lead and cadmium–mobilized primarily through automobile emissions and industrial processes–are ubiquitous in our environment.[1] Although the neuropsychological impairments associated with lead and cadmium poisoning are well established, increasing interest has been shown in the potential sub-clinical behavioural effects of low-level exposures to these toxic metals. Attention, in particular, has been paid to the links between lead and cadmium exposures and diminished cognitive functioning,[2-4] learning disabilities,[5,6] hyperactivity,[7] and attention-deficit behaviours.[8]

Results reported from the Ontario Child Health Study suggest that over 10% of children aged 4 to 11 years suffer from an emotional disorder.[9] In spite of their apparent importance, such 'internalizing' problems remain relatively understudied with respect to their potential association with sub-toxic exposures to lead and/or cadmium. Results obtained in studies undertaken by Marlowe at al.[10] and Kracke[11] suggest the potential aetiological importance of toxic metal exposures in emotional problems, and highlight the need for further research.

This study aims to assess the relationship between toxic metal exposures and the emotional well-being of children. More precisely, the associations between hair lead and cadmium levels and specific depressive and anxiety-related symptomology in children are examined.

Materials and Methods

Study Population: The research discussed in this paper was undertaken using data collected during the period October to December, 1997, as part of a larger study of children's mental health. The study, described in detail elsewhere,[12] employed a cross-sectional design, and targeted children attending grades K through 4 at 15 Englishlanguage public elementary schools located in the heart of the Victoria Census Metropolitan Area (British Columbia, Canada). Fourteen of the schools agreed to participate in a follow-up study which involved the collection of hair samples necessary for the present study.

Permission was obtained to collect hair samples from 327 children. Of these children, 42 had hair which was too short to sample,

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and 27 were unavailable or withdrew consent at the time of collection. Of the 258 children from whom hair samples were successfully collected, 21 (8.1%) had an existing condition (physical disability, neurological disorder, or learning disability) which may represent a 'probable cause' for behavioural disturbance. These children were omitted from the sample for the purposes of the present investigation; the remaining 237 children were retained for further analysis.

Psychometric Measures: Information about the presence of the depressive and anxiety-related symptomology considered was derived from parental responses to the Walker Problem Behaviour Identification Checklist,[13] a behavioural assessment tool which consists of 50 items describing negative behaviours. Parents were asked to select those items which were characteristic of their child's behaviour in the preceding two month period. The 12 Walker items selected for use in this study (Table 1, p.99) were intended to reflect specific maladaptive behaviours consistent with the general patterns of symptomology identified for a number of anxiety and depression-related disorders;[14-16] including feelings of mistrust and worry, somatic complaints, nightmares, repetitive behaviours, impaired concentration, instability of mood, sadness, and low self esteem.

Socio-Demographic Status Measures: Parental responses to a survey questionnaire provided information about each child's age and sex, family composition, socio-economic status, and housing situation. Of particular interest for the purposes of the present investigation were other factors which may influence behavioural well-being, measured as dichotomous variables indicating whether the child:

1) had a biological parent who had ever been treated for a mental illness
2) lived in a single parent family
3) was born to a mother under 20 years of age
4) lived in a family of low socio-economic status (family income less than $20,000/year and/or living in subsidised housing)
5) experienced a stressful life event in the preceding 6 month period (a family member or pet died; a family member moved away from home).

Classification of Metal Levels: While body stores of a wide range of toxic and essential elements can be ascertained using a number of tissues, including blood, urine, teeth, and organ samples, scalp hair is increasingly considered a more desirable biopsy material for this purpose. As an excretory tissue, hair incorporates atoms of individual elements during its growth cycle and, because following its formation it is isolated from the body's ongoing metabolic activities,[17] it provides a permanent record of the levels of those elements in the body at the time of growth. While both blood and urine can be used to measure the concentration of particular elements in the body, they reflect only what was in the system at the time of, or in the hours preceding collection, and are therefore subject to a high degree of shortterm variability. Concentrations of elements in hair, on the other hand, provide a measure of average exposure over the time period in which the hair was grown.[18] With an average hair growth rate of about one centimetre each month,[19] a sample comprised of the three centimetres of most recent growth will typically provide a measure of average exposure over the preceding three month period. Human hair has been demonstrated to reflect environmental exposures to both cadmium[20-22] and lead.[20, 23-25] As well, significant direct correlations have been observed between hair lead levels and those measured in blood[24,26] and bone[27] amongst those occupationally or environmentally exposed. Hair samples were obtained from the participating children during normal school hours. Proximal samples of approximately 2.5 centimetres in length were collected, to a mass in excess of 250 milligrams, from approximately 10 sites at the nape of the neck using clean, stainless steel scissors. Samples were submitted for analy-

Table 1. Walker items used in this study.

Symptom	Walker Item	Behavioural Descriptor
Mistrust and worry	16	Makes distrustful or suspicious remarks about actions of others toward him/her.
	36	Expresses concern about something terrible or horrible happening to him/her.
Somatic complaints	2	Is listless and continually tired.
	17	Reacts to stressful situations or changes in routine with general body aches, head or stomach aches, nausea.
Nightmares	33	Complains of nightmares, bad dreams.
Repetitive Behaviours	23	Utters nonsense syllables and/or babbles to himself/herself.
	26	Repeats one idea, thought, or activity over and over.
Impaired concentration	9	Has difficulty concentrating for any length of time.
		Instability of mood, sadness, and low self-esteem
	28	Refers to himself/herself as dumb, stupid or incapable.
	31	Has rapid mood shifts: depressed one moment, manic the next.
	34	Expresses concern about being lonely, unhappy.
	47	Weeps or cries without provocation

sis to Doctor's Data, Inc., a licensed medical laboratory located in St. Charles, Illinois.

Upon receipt of the hair samples, technicians cut the specimens into pieces approximately 0.3 centimetres in length and mixed them to allow for a representative subsampling of the hair. In order to remove exogenous contaminants, samples were washed (four times) in a non-ionic detergent, rinsed in acetone, and in de-ionised water (three times). Hair specimens were again rinsed in acetone (twice) before drying in an oven at 75±5°C. The dry samples were digested in nitric acid and analysed for element content in an inductively coupled plasma-mass spectrometer (ICP-MS). To ensure valid element determinations, calibration verifications, a certified hair control, in house hair controls, spiked hair samples, and other appropriate control samples were tested.[28] Results of the hair analyses were reported in parts per million (ppm).

Theoretical normal levels for the toxic metals considered in this study have been established by Doctor's Data, Inc. using literature values, patient populations, and other laboratories' reference ranges; and subsequently validated by a physician-defined "healthy" population.[29] The reference ranges were used to categorise the children as "high exposed" to the metals in question if the concentration in their hair was greater than the upper limit of the 'normal' range (0.70ppm for lead; 0.25ppm for cadmium).

Statistical Analyses: Statistical analyses were undertaken in two stages. The first stage in the analysis was performed in order to evaluate the relationship between the dichotomous variables indicating hair metal status ('high exposed' or 'normal') and the presence or absence of each behavioural descriptor considered. Analyses of 2X2 contingency tables were used to statistically compare the frequency of 'high' exposure to each element amongst those children who had the maladaptive behaviour (Group 1) versus those who did not (Group 0). The statistical significance of the bivariate associations between the hair metal and behaviour- related variables was ascertained using continuity-corrected chi-square values and their associated probabilities, while the strength and direction of the observed associations were reported in terms of odds ratios. In order to further evaluate the significant relationships between hair metal status and behaviour identified in the first analytical phase, multivariate logistical regression analyses were used to assess the strength and direction of the associations between the response (behavioural descriptor) and explanatory (hair metal status) variables, while controlling for the influence of other potential explanatory factors such as age, sex, social status, and stressful life events. As with the bivariate analyses, the strength and direction of the observed associations are reported as odds ratios.

Results

Hair Metal Status: Comparison of the hair analysis results with the laboratory reference ranges revealed that a total of 24 (10.1%) of the children had elevated hair lead levels. Cadmium exposures which fell outside of the normal range were less common in the sample, with a rate of "high" exposure of 5.5% (13 of the children). For both metals, the observed rate of "high" exposure was significantly associated with subject sex. For lead, five females (4.1%) were high exposed, while 19 (16.7%) of the males had 'high' hair concentrations of the element (phi=0.209; $p.<0.01$). For cadmium, two of the female subjects (1.6%) were high exposed, compared to 11 (9.6%) of the males (phi=0.292; $p.<0.0001$). As well, a significant direct association was observed between cadmium and lead status, wherein children 'high' exposed to one of the metals were significantly more likely than other children to be 'high' exposed to the other (phi=0.349; $p.<0.0001$).

Prevalence of Maladaptive Behaviours: The frequency of selection for each Walker item considered is shown in Table 2. (p. 101) Three of the items ("is listless and continually tired," "has rapid mood shifts: depressed one moment, manic the next," and "weeps or cries without provocation"), were selected for only six (2.5%) of the children. Given the low prevalence of these behaviours in the sample, they were excluded from further analysis. For eight of the remaining items, the rate of selection by parents was higher for males than for females. For three of these ("makes distrustful or suspicious remarks about actions of others toward him/her"; "expresses concern about something terrible or horrible happening to him/her"; "utters nonsense syllables and/or babbles to himself/herself "), chi-square analyses of 2X2 contingency tables revealed that the apparent disparities between male and female prevalence rates were statistically significant. For a single behavioural descriptor–the item describing somatic complaints–the prevalence rate in the sample was higher for females than for males, but not significantly so.

Bivariate Analyses: Results of the bivariate analyses–comparing the rate of 'high' exposure amongst those who have the discrete behavioural problem in question versus those who do not–are shown in Table 3 (p.102). A total of four of the behavioural descriptors considered were significantly associated with one or both of the hair metal status variables. In each case, the rate of 'high' exposure to the elements in question was significantly higher amongst those children with the maladaptive behaviour (Group 1) than those without (Group 0). For the first of these–"makes distrustful or suspicious remarks about actions of others toward him/her"–there was a marked,

Table 2. Prevalence of maladaptive behaviours.

Walker Item	Prevalence (sample) n (%)	Prevalence (males) n (%)	Prevalence (females) n (%)	Continuity Corrected X2
Makes distrustful or suspicious remarks about actions of others toward him/her	12 (5.1	10 (8.8)	2 (1.6)	4.886*
Expresses concern about something terrible or horrible happening to him/her	14 (5.9)	12 (10.5)	2 (1.6	6.907**
Is listless and continually tired	6 (2.5	2 (1.8)	4 (3.3)	0.102
Reacts to stressful situations or changesin routine with general body aches, head or stomach aches nausea	47 (19.8)	19 (16.7)	28 (22.8)	1.027
Complains of nightmares bad dreams	47 (19.8)	25 (21.9)	22 (17.9)	0.381
Utters nonsense syllables and/or babbles to himself/herself.	13 (5.5)	12 (10.5)	1 (0.8)	8.975**
Repeats one idea, thought, or activity over and over.	16 (6.8)	11 (9.6)	5 (4.1)	2.111
Has difficulty concentrating for any length of time.	29 (12.2)	17 (14.9)	12 (9.8)	1.024
Refers to himself/herself as dumb, stupid or incapable.	41 (17.3)	23 (20.2)	18 (14.6)	0.912
Has rapid mood shifts: depressed one moment, manic the next.	6 (2.5)	3 (2.6)	3 (2.4)	0.000
Expresses concern about being lonely, unhappy.	20 (8.4)	11 (9.6)	9 (7.3)	0.169

*p<0.05 **p<0.01

statistically significant difference in the rate of "high" exposure to each element. Rates of "high" exposure to both lead and cadmium also occurred significantly more frequently in children with somatic complaints ("reacts to stressful situations or changes in routine with general body aches, head or stomach aches, nausea"), and in those who utter nonsense syllables and/or babble to themselves. As well, children expressing anxiety about the occurrence of terrible or horrible events were significantly more likely than other children to be "high" exposed to lead.

Multivariate Analyses: A total of four three-stage hierarchical logistic regression models were estimated; one for each behavioural descriptor which, according to the results of the bivariate analyses, had a significant association with one or both of the hair metal status variables. In the first stage, the hair metal variables identified as significant in the bivariate analyses were entered into the models in a forward stepwise fashion. Criteria for entry into the models was based upon the significance of the Wald statistic (p.[in]=0.05; p.[out]=0.10). In the second stage, the variables describing other factors which may influence behavioural well-being (such as social status) were entered into the models, also in a forward step-wise fashion. In the final stage, variables pertaining to age and sex were forced into the models; the latter variable intended to control for potential confounding effects suggested by the significant relationships between subject sex and both

Table 3. Chi-Square analysis results.

Walker Item	Pb % High Exposed Group 0/Group 1 (X2; Odds Ratio)	Cd % High Exposed Group 0/Group 1 (X2; Odds Ratio)
Makes distrustful or suspicious remarks about actions of others toward him/her.	8.4 / 41.7 (10.407**; 7.744)	4.4 / 25.0 (5.743*; 7.167)
Expresses concern about something terrible or horrible happening to him/her.	7.6 /50.0 (21.545**; 12.118)	4.9 / 14.3 (0.785; 3.212)
Reacts to stressful situations or changes in routine with general body aches, head or stomach aches, nausea.	7.4 / 21.3 (6.553*; 3.398)	3.7 / 12.8 (4.371*; 3.826)
Complains of nightmares, bad dreams.	8.9 / 14.9 (0.883; 1.781)	4.2 / 10.6 (1.891; 2.708)
Utters nonsense syllables and/or babbles to himself/herself.	8.9 / 30.8 (4.264*; 4.533)	4.5 / 23.1 (5.013*; 6.429)
Repeats one idea, thought, or activity over and over.	9.5 / 18.8 (0.570; 2.198)	4.5 / 18.8 (3.403; 4.869)
Has difficulty concentrating for any length of time.	10.1 / 10.3 (0.000; 1.027)	4.3 / 13.8 (2.763; 3.538)
Expresses concern about being onely, unhappy.	9.2 / 20.0 (1.305; 2.463)	5.1 / 10.0 (0.171; 2.081)
Refers to himself/herself as dumb, stupid or incapable.	8.2 / 19.5 (3.633; 2.727)	9.8 / 4.6 (0.890; 2.246)

*p<0.05 **p<0.01

hair metal and behavioural status. Results for the multivariate analyses are summarised in Tables 4 through 7.

In the first stage of the multivariate analysis for the behavioural descriptor "makes distrustful or suspicious remarks about the actions of others toward him/her," (Table 4, below) a single metal status variable–"high" lead–entered the model. The addition of other potential explanatory or confounding variables in the subsequent stages of the model (the variable describing low socio-economic status in the second stage, and the statistically insignificant entry of the age and sex variables in the third stage) only slightly attenuated the magnitude and statistical significance of the odds ratio corresponding to the lead status variable: after controlling for the effects of the other variables, children with the maladaptive behaviour in question were almost six times as likely as other children to be "high" exposed to lead (O.R.=5.777; p.<0.05).

As shown in Table 5, (p. 104) the previously observed association between hair lead status and expressions of anxiety about the occurrence of terrible or horrible events is confirmed by the results of the multivariate analyses. Entry into the model of additional variables in subsequent stages–including factors indicating a recent stressful event, subject sex, and (the statistically insignificant effect of) subject age–reduced, but did not render statistically insignificant, the magnitude of the association between hair lead status and the behavioural descriptor in question (from O.R.=12.117; p.<0.01 in the first stage to O.R.=9.885; p.<0.01 in the final stage).

Results obtained in the bivariate analyses suggested significant statistical relationships between both lead and cadmium status and somatic complaints. Results of the multivariate analyses (Table 6, p. 104) reveal that when controlling for the "shared" effects of the metal status variables, only lead is of (statistical) concern, with those children "high" exposed to the metal over three times as likely as other children to have such somatic symptomology (O.R.=3.397; p.<0.01). In subsequent stages of the model, the strength of the association between lead status and the behavioural descriptor variable increased slightly (to O.R.=4.701; p.<0.01 in the final stage of the logistic regression model). The factor describing a recent stressful event was the only other significant predictor identified for this specific maladaptive behaviour.

For the remaining behavioural descriptor –"utters nonsense syllables and/or babbles to himself/herself "–the hair cadmium variable

Table 4. Logistic regression analysis results–Makes distrustful or suspicious remarks about actions of others toward him/her.

Stage 1	Stage 2	Stage 3
Variable (Odds Ratio)	Variable (Odds Ratio)	Variable (Odds Ratio)
High Lead (7.744**)	High Lead (8.772**) Low SES (6.672**)	High Lead (5.777*) Low SES (7.540**)
		Age (1.173) Male Sex (4.862)

*p.<0.05**p.<0.01

was significantly associated with behavioural status in the first stage of the model (Table 7, p.105). However, the confounding effect of subject sex alone significantly reduced the association between cadmium exposure and the maladaptive behaviour in question (from O.R.=6.420; p.<0.05 in stage 1, to O.R.=3.756; p.>0.05 in stage 3).

Discussion

A number of specific maladaptive behaviours considered in this paper were significantly associated with toxic metal exposures, both before and after considering the effects of social and family status, stressful life events, subject age, and subject sex. Although the use of cross-sectional data and a volunteer sample preclude the advancement of causal statements, the findings reported here are suggestive of processes which merit further consideration.

Lead exposure figured prominently in the results obtained in both the bivariate

Table 5. Logistic regression analysis results–Expresses concern about something terrible or horrible happening to him/her.

Stage 1	Stage 2	Stage 3
Variable (Odds Ratio)	Variable (Odds Ratio)	Variable (Odds Ratio)
High Lead (12.117**)	High Lead (14.765**)	High Lead (9.885**)
	Stressful Event (3.663*)	Stressful Event (3.980*)
		Age (0.996)
		Male Sex (5.266*)

*p.<0.05 **p.<0.01

Table 6. Logistic regression analysis results–Reacts to stressful situations or changes in routine with general body aches, head or stomach aches, nausea.

Stage 1	Stage 2	Stage 3
Variable (Odds Ratio)	Variable (Odds Ratio)	Variable (Odds Ratio)
High Lead (3.397**)	High Lead (3.661**)	High Lead (4.701**)
	Stressful Event (2.083*)	Stressful Event (2.001*)
		Age (0.976)
		Male Sex (0.534)

*p.<0.05**p.<0.01

and multivariate analyses. Although considerable symptomatic overlap exists between depressive and anxiety-related disorders in children, three of the behaviours in question–"makes distrustful or suspicious remarks about actions of others toward him/her," "expresses concern about something terrible or horrible happening to him/her," and "reacts to stressful situations or changes in routine with general body aches, head or stomach aches, nausea" –appear particularly consistent with the patterns of symptomology associated with anxiety disorders.

The results obtained for cadmium suggest that sub-toxic exposures to the metal did not make a unique contribution to the behavioural outcomes considered in this study. In one instance, the significance of the cadmium status variable was obviated by the confounding effect of subject sex. For the remaining multivariate analyses in which it was considered, cadmium status appeared–as a result of its significant association with lead status– to serve as a proxy for the stronger effect associated with the lead exposure variable. The significant relationship between lead and cadmium exposure observed in the present study is consistent with findings reported elsewhere.[2,3,30] However, given that the analytical methods employed in this study were unable to separate the individual effects of such closely related variables (or to identify their potential interactive effects), and given the suggestion that lead levels may act as a marker for the toxic effects of cadmium,[31] the potential importance of low-level cadmium exposure is not easily discounted.

In sum, the results reported here highlight the potential impact of low level lead exposures on the emotional well-being of children, and call further into question the notion of "safe" levels of exposure to toxic metals.

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Table 7. Logistic regression analysis results–Utters nonsense syllables and/or babbles to himself/herself.

Stage 1	Stage 2	Stage 3
Variable (Odds Ratio)	Variable (Odds Ratio)	Variable (Odds Ratio)
High Cadmium (6.420*)	High Cadmium (6.420*)	High Cadmium (3.756)
		Age (0.981)
		Male Sex (12.219*)

*p.<0.05 **p.<0.01

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