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Lead Exposure and Visual-Motor Abilities in Children from Chennai, India

Kavitha Palaniappan[1], **Ananya Roy**[2], **Kalpana Balakrishnan**[1], **Lakshmi Krishnan**[1], **Bhramar Mukherjee**[3], **Howard Hu**[4,5,6], and **David C. Bellinger**[6,7]

[1] Department of Environmental Health and Engineering, Sri Ramachandra Medical College and Research Institute, Chennai, India

[2] Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ

[3] Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, MI

[4] Department of Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, MI

[5] Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

[6] Department of Environmental Health, Harvard School of Public Health, Boston, MA, USA

[7] Department of Neurology, Children's Hospital, Harvard Medical School, Boston, MA, USA

Abstract

Lead exposure poses a major environmental hazard in India, but little information is available on the impact of lead exposure on neurobehavioral development in Indian children. We hypothesize that higher blood lead levels are associated with poorer visual-motor, visual-spatial and fine motor functioning among children. We conducted a cross-sectional study of 814 school children, aged 3–7 years. Lead in whole blood was measured using the LeadCare Analyzer. The Wide Range of Visual Motor Abilities Test (WRAVMA) was administered to each child by trained examiners. The mean blood lead level was 11.4 ± 5.3 μg//dL. In multivariate analyses adjusting for mother's education level, fathers education level, average monthly income, hemoglobin and sex, WRAVMA scores were inversely related to blood lead level. An increase of 10 μg/dL was associated with a decrease of 2.6 points (95% CI: −4.5 to −0.7, P=0.006) in the Visual Motor Composite score and a decrease of 2.9 points (95% CI: −5.1 to −0.7, P=0.011) in the Drawing subtest. Exploration of the shape of the dose-effect relationships using spline functions indicated some non-linearities, with the steepest declines in visual-motor skills occurring at higher blood lead levels. Among urban Indian children, higher blood lead levels are associated with decreased visual-motor abilities, particularly visual-motor integration.

Keywords

Lead levels; visual motor abilities; children

Corresponding Author: Ananya Roy, Sc.D., M.Sc., Environmental Epidemiology and Statistics, Environmental and Occupational Health Sciences, Institute, Room 358, 170 Frelinghuysen Road, Piscataway, NJ 08854, aroykaushik@gmail.com, Tel: 617 642 0963.

1. INTRODUCTION

Lead exposure poses a major environmental health problem in India. In a 7-city screening survey (1), 53% of children less than 12 years of age had blood lead levels of 10 μg/dL or greater (the level of concern set by the U.S. Centers for Disease Control and Prevention since 1991). Similarly, the National Health and Family Survey in India (1998–1999), found that 45% and 50% of children, in Delhi and Mumbai respectively, had blood lead levels higher than 10 μg/dl (2). Even though lead was subsequently phased out of gasoline in India in a process completed in 2001, blood lead levels have tended to remain high. For example, blood lead level exceeded 10 μg/dl in 37% of children in Mumbai in 2002–2003 (3) and >50% of children in Chennai in 2003 and 2006 (4, 5).

With regards to health impacts, little research has been conducted in India on the potential of such lead exposure to influence the neurodevelopment of children. Nevertheless, in undertaking new research on this subject, opportunities exist to not only to study such impacts using psychometrics employed in many other such studies around the world, but to also continue the exploration of the nuances of lead's impact with more precise tools.

In considering the many studies over the past three decades that have focused on characterizing the neurobehavioral effects of lead on children, little success has been achieved in identifying an invariant "behavioral signature" of increased exposure. One of the more consistent observations is that children's blood lead levels are inversely associated with performance on tests that focus on visual-motor ability (6).

Because visual-motor ability is a multi-dimensional construct, strong inferences cannot be drawn about the specific aspects of visual-motor ability that are most vulnerable to lead unless the tests used to assess different aspects are equivalent in sensitivity. It is difficult to meet this criterion unless a test is used that consists of co-normed subtests that assess different aspects of such abilities. The primary objective of this study was to use such a test, the Wide Range Assessment of Visual Motor Abilities (WRAVMA), to determine whether the adverse effects of increased lead differ with respect to visual-motor (figure copying), visual-spatial (matching designs), and fine-motor (pegboard) skills.

2. METHODS

This study was approved by the Indian Council of Medical Research, Inter-Ministerial and Health Ministry Screening Committee of India, the Medical Ethics Committee of Sri Ramachandra University, and the Human Subjects Committees of the Harvard School of Public Health and the University of Michigan.

2.1. Research Design

This was a cross-sectional epidemiological study of children aged 3–7 years attending public schools in the area of Chennai. Four zones of varying industry and traffic levels (high traffic/low industry, high traffic/high industry, low traffic/ high industry and low traffic/low industry) were selected on the basis of zoning information provided by the Tamil Nadu State Pollution Control Board and the Chennai city traffic police department. Within each zone, three schools were selected (12 schools in all) and, from these, 3–7 years old children were recruited into the study. Initially, 814 children were enrolled in the study, but 58 children were absent from school or sick on the day of blood collection, leaving a total of 756 participants (92.8%). Informed consent was obtained from the primary caregiver of the child and blood lead levels obtained over a period of three years, from 2003 to 2006.

2.2. Primary Socio-demographic Data

Data were collected from each child's parent or primary caregiver (mother, in most cases) using a questionnaire that covered topics related to the child's birth history, birth rank, infant-feeding history, child's age at testing, gender, school, parents' education and occupation, socio-economic background of the family (assessed using the Kuppuswamy's Socio-Economic Status Scale (Urban), revised in 2001 to reflect current wage scales) (7), maternal age at delivery, family size, living conditions (overall health, food habits, intake of alcohol, passive smoking), nutritional and dietary habits of the child (intake of milk, red meat, fish, eggs, ragi, jaggery, green vegetables and fruits), use of dietary supplements (calcium and iron), medical details (use of ayurvedic, herbal, homeopathic and other alternative medicines), and environmental surroundings (industrial exposure, traffic exposure, hobbies, residential exposure from paints and toys).

2.3. Anthropometric Measurements

Measurements were made of a child's height (in centimeters), weight (in kilograms), and arm circumference (in centimeters). A pediatrician conducted a general physical examination, including observation for signs of mild ataxia, bilateral wrist drop, and Burton's line at the base of the gums.

2.4. Wide Range Assessment of Visual Motor Abilities

The Wide Range Assessment of Visual Motor Abilities (WRAVMA) (8) was administered to each child in a small, quiet, comfortable room on school premises. Instructions were given to the child in Tamil, the local language. The three examiners were blinded to all aspects of the children's lead exposure and developmental histories. As a souvenir, a child was given a small case filled with stationary and other useful items.

The WRAVMA consists of three subtests, Drawing, Matching, and Pegboard, selected because of their relevance to school activities. All were normed on the same standardization sample, thus permitting valid comparison of subtest scores. Each subtest yields a standard score, which has an expected mean of 100 and a standard deviation of 15. The three subtests are as follows:

Drawing (Visual-Motor)—On the Drawing task, the child was asked to copy designs which were arranged in order of increasing difficulty. Starting at an age-appropriate item, the child proceeded until three consecutive items were failed.

Matching (Visual-Spatial)—The Matching task assesses spatial skill by presenting tasks arranged in order of increasing difficulty. Starting at an age-appropriate item, the child marked which of four options "goes best" with the standard item. Making the correct choice in each test item was heavily dependent upon various visual-spatial skills such as perspective, orientation, rotation, figure-ground, spatial symmetry, size discrimination, etc. The child continued until he or she made six errors in a series of eight consecutive items.

Pegboard (Fine Motor)—On the Pegboard task, the child inserted as many round pegs as possible within 90 seconds. Two trials were administered. On the first, a child used the dominant hand (defined as the hand the child uses to write or draw), followed by a second trial using the non-dominant hand. The dominant hand score is used to calculate the Fine Motor standard score.

Visual-Motor Abilities Composite—Standard scores on the three subtests were combined to yield a Composite standard score.

2.5. Blood Collection and Measurement of Blood Lead Level

After a child's puncture site was washed with 100% isopropanol, a 10 ml blood sample was drawn from the antecubital vein and collected into a lead-free vacutainer (royal blue top tubes #369736, Becton-Dickinson, Franklin Lakes, NJ USA). Lead in whole blood was measured using the LeadCare Analyzer (ESA Laboratories, Chelmsford (formerly Bedford), MA, USA), a well-validated field instrument with sensitivity of 1 μg/dL (9). Kit controls and duplicates were run every 20 samples and with every change in test kit batch. The equipment was recalibrated with every batch.

2.6. Statistical Analyses

Basic descriptive summaries of quantitative variables were examined in terms of measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range). For categorical variables, sample frequency distributions were examined

Linear associations between blood lead levels and standardized scores on three WRAVMA subtests and the Composite score were assessed by calculating Pearson correlation coefficients and by fitting bivariate linear regression models. Multivariate linear regression models were also fitted, adjusting for gender, age, hemoglobin level, average monthly income of the family and parent education. Average monthly income was categorized into three classes (<4000, 4000–6500 and above 6500 Rs per month). Parental education was categorized into four categories (illiterate or primary school only, middle school completion, high school certificate, post high school). These categories were chosen so that at least 15% of the total number of observations fell in each category.

All analyses are based on the 755 children for whom complete information was available on all the variables included in the multivariate regression models. Because blood lead levels were skewed to the right, log-transformed values were also evaluated. Results were similar, so for ease of interpretation, we present results of models using untransformed blood lead levels.

Since the study had a nested hierarchical sampling structure, the intra-class correlation of visual-motor ability scores at each level (zone, school, class) was examined using random effects mixed models. As the covariance within the levels did not fit a specified structure, we chose to account for the clustering of observations in the marginal models using generalized estimating equations (GEE) which utilize quasi-likelihood methods for estimation (10). All reported effect estimates account for clustering at the school and classroom levels.

We explored the shape of the association between blood lead level and WRAVMA scores by allowing our model to have different slopes within different ranges of blood lead. In addition, nonparametric regression models were fitted using generalized additive mixed models (GAMM). In the adjusted regression model, a smooth functional term corresponding to blood lead was used instead of just a linear term, which allowed us to identify potential non-linear associations between blood lead level and WRAVMA scores. The smoothing term was fitted using penalized regression splines, with the degree of smoothness selected by cross-validation technique.

Care was taken to ensure that the results were not unduly influenced by the data of individual children or extreme observations. Diagnostics to identify outliers and influential observations were computed, and models were re-fitted after removing observations that exerted even moderately significant influence on the overall analysis. Because the findings were did not differ appreciably when outliers or influential observations were deleted, we present analyses based on all available observations.

Statistical analyses were performed using SAS for Windows, version 9.2 (SAS Institute Inc., Cary, NC) and R version 2.5.1 (www.r-project.org).

3. Results

Table 1 provides descriptive information about the sample. The summaries are based on available complete information on the 814 subjects, after ignoring missing data. Approximately half (53%) of the children were male. With regard socio-economic status, 73% of families belonged to the middle class, 23% to the lower class, and 4% to the upper class. Most children (98%) resided with their parents. The mean birth weight was 2832 grams (SD: 512). The average maternal age at delivery was 24 years (SD: 4). About 56% of the subjects' parents had completed school education (12 years of education). The mean blood lead level was 11.5 μg/dL (standard deviation: 5.3, range: 2.6–40.5). Approximately half (52.5%) of the children had a blood lead level greater than 10 μg/dL.

The Pearson correlation coefficients between blood lead level and WRAVMA Drawing, Matching, Pegboard and Composite score were −0.12 ($p=0.001$), −0.10 ($p=0.006$), −0.06 ($p=0.07$) and −0.12 ($p=0.001$) respectively, indicating modest inverse associations with all three. Table 2 presents the results of bivariate regressions of WRAVMA scores on blood lead level, and Figure 1 presents graphical descriptions of these associations.

After adjusting for the covariates (gender, maternal education, average monthly income of the family and hemoglobin), a 10 μg/dL increase in blood lead level was associated with a decrease of 2.9 points (95% CI: 0.7, 5.1) in WRAVMA Drawing score and a decrease of 2.6 points (95% CI: 0.7, 4.5) in WRAVMA Composite score (Table 3). Family income, maternal education, and hemoglobin were significant predictors of one or more WRAVMA scores, but sex was not.

The nonparametric regression (GAMM) models, adjusted for covariates and clustering, revealed significant non-linearity in the relationship between blood lead level and the WRAVMA Drawing score (Figure 2). The greatest decline seemed to occur at blood lead levels greater than 30 μg/dL. The association between blood lead level and Pegboard score, as well as Matching score appeared to be linear across the entire range of blood lead level. Table 4 presents the results for the smoothing term for blood lead in the adjusted GAM models of the four WRAVMA scores.

4. Discussion

As in other surveys taken in India following the phase-out of lead in gasoline in 2001, our study found that blood lead levels in children remain relatively high, with half (52.5%) of the children having a level greater than 10 μg/dL. By itself, this finding indicates the need for exposure assessment research that can detail likely sources and pathways of exposure to lead that, in turn, can inform efforts at exposure prevention.

The significant inverse relationship we observed between blood lead level and the Drawing score on the WRAVMA is consistent with existing literature. In a pilot study in Chennai, we found that a 10 μg/dL increase in concurrent blood lead among 4 to 14 year olds was associated with a 6 point decrease in WRAVMA Composite score (4). Among preschool-age children, on tests that assess multiple domains of abilities, scales that assess nonverbal skills tend to be the ones on which scores are most strongly associated with lead. For instance, in the Boston (11), Port Pirie (12), and Kosovo (13) prospective studies , this was the Perceptual-Performance scale of the McCarthy Scales of Children's Abilities. In the Cincinnati prospective study, it was the Simultaneous Processing Scale of the Kaufman-Assessment Battery for Children (14).

Several studies have reported significant inverse associations between lead levels and performance on design copying tasks similar to the Drawing subtest of the WRAVMA, the subtest score that was most strongly associated with blood lead level. These tests include the Developmental Test of Visual-Motor Integration (15–17), the Rey-Osterrieth Complex Figure Test (18)and the Bender-Gestalt test (19), . Winneke (1996) suggested that visual-motor integration is more consistently associated with increased lead exposure than is psychometric intelligence (20).

Finally, some studies have reported that higher blood lead levels impair fine-motor skills (16, 17, 21). Dietrich et al. (1993) also found that higher blood lead levels were associated with lower scores on bilateral coordination, visual-motor control, and upper-limb speed. Gross motor skills appear to be less affected than are fine motor skills (16, 21).

We found evidence of non-linearity in the dose-effect relationship between blood lead level and WRAVMA Drawing scores, but not of the supralinear (i.e., log-linear) form that has been reported in several studies for the relationship between blood lead level and IQ scores (22–24) and general cognitive development (25, 26). In those studies, the inverse slope was steeper at lower rather than at higher blood lead levels. In contrast, we found a suggestion that, for WRAVMA scores, the slope was steeper at higher than at lower levels. The explanation for this discrepancy is not obvious. The functional form of the relationship might be endpoint-specific, although this seems unlikely, or differ depending on factors such as lead exposure history, genotype, nutrition, or the social environment.

This study has several limitations. First, it was cross-sectional in design, and information was available only on a child's concurrent blood lead level. If it is lead exposure in the first few years of life that is most hazardous to a child's development, this could have resulted in exposure misclassification in view of the relatively short exposure averaging period of blood lead. On the other hand, recent studies suggest that a blood lead level measured at school-age is the level that is most strongly predictive of neuropsychological outcomes such as IQ (22). Second, it is not possible to conclude, with confidence, that it is specifically impaired visual-motor integration that underlies the difficulty more highly exposed children have on design copying tasks such as the Drawing subtest of the WRAVMA. This is because good performance requires the effective coordination of multiple skills, including grapho-motor control, attention, motivation, and planning. To identify the specific deficit would require assessments that isolate and evaluate the requisite component skills. A third limitation is the absence of normative data on the WRAVMA for Indian children, which precludes drawing inferences about the clinical implications of the lead-associated decrements observed. The children's standard scores on the Drawing subtest were higher than those expected based on the U.S. standardization sample, but the children's standard scores on the Matching subtest were considerably lower. Perhaps this reflects different areas of emphasis in Indian and U.S. education of young children, but this is speculation.

In summary, in developed countries childhood lead exposure is on the decline due to implementation of environmental and occupational regulations (27). Lead poisoning continues to be a serious problem in developing countries, however (28, 29). Without appropriate primary prevention, lead exposure will remain a threat to future generations of children in the developing world.

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Units and Abbreviations

µg/ dL	microgram per deciliter
WRAVMA	Wide Range Assessment of Visual Motor Abilities
GEE	Generalized Estimating Equations
GAMM	Generalized Additive Mixed Models

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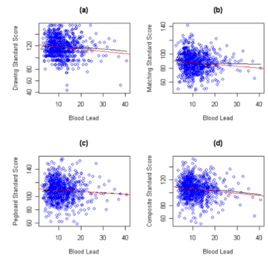

Figure 1.

Scatter plots of WRAVMA scores (Drawing, Matching, Pegboard, Composite) and blood lead level, with fitted least squares line (red) and locally smoothed line (black)

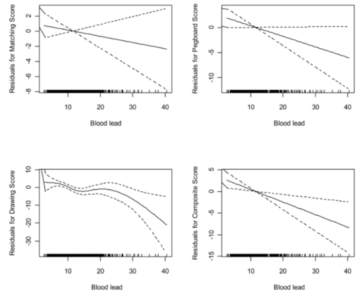

Figure 2.

Smooth functional term relating WRAVMA scores to blood lead in an adjusted Generalized Additive Mixed Model, adjusting for gender, average monthly income, hemoglobin and parents' educational level and clustering at school and class level.

Table 1

Descriptive statistics for the variables included in data analysis For continuous variables Mean ± SD, Median ± IQR, Range and for categorical variables, relative frequencies in each category are presented.

Variable	Summary measures	
Gender		
Male	53.3%	
Female	46.7%	
Average Monthly income (in Rs)		
<2000	15.5%	
2000–4000	43.5%	
4000–6500	24.8%	
6500–13000	10.9%	
>13000	5.3%	
Education level:	Mother's	Father's
Illiterate	5.7%	3.1%
Primary School or Literate	12.3%	9.2%
Middle School Completion	33.7%	28.1%
High School Certificate	24.2%	28.3%
Post High School Diploma	9.9%	11.9%
Bachelors Degree	11.3%	14.3%
≥Masters/Professional Degree	2.9%	5.1%
Hemoglobin	11.9±1.2	
	12± 1.5; Range (5.2, 16.9)	
Blood lead concentration (μg/dl)	11.5±5.3	
	10.3±6.3; Range (2.6, 40.5)	
WRAVMA Scores		
Drawing standard score	117.57±16.84	
	117.5±20; Range (43,155)	
Matching standard score	87.62±13.77	
	88±18; Range (47,141)	
Pegboard standard score	108.04±15.45	
	108±21; Range (59,155)	
WRAVMA composite score	105.38±15.31	
	105.5±19.5; Range (52,152)	

Table 2

Unadjusted* effect of lead on WRAVMA scores

WRAVMA Scores	Estimate	p-value	Confidence Interval	
Drawing standard score	−0.38	0.001	−0.62	−0.15
Matching standard score	−0.26	0.013	−0.46	−0.05
Pegboard standard score	−0.19	0.058	−0.39	0.01
Composite standard score	−0.35	0.001	−0.56	−0.15

*Accounting for clustering at school and class level

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Table 3

Association between blood lead and WRAVMA from multivariate generalized estimating equations*

WRAVMA Scores	Estimate	p-value	Confidence Interval	
Drawing standard score	−0.29	0.011	−0.51	−0.07
Matching standard score	−0.14	0.093	−0.31	0.02
Pegboard standard score	−0.19	0.062	−0.38	0.01
Composite standard score	−0.26	0.006	−0.45	−0.07

*Controlling for sex, hemoglobin level, mother's education level, father's education level and average monthly income of the family, and accounting for clustering at school and class level.

Table 4

Adjusted generalized additive mixed models[#] on the smoothing term for blood level

Response	Effective DF[*]	F statistic	p-value[**]
Drawing Score	3.58	4.03	0.002
Matching Score	1.00	0.52	0.543
Pegboard Score	1.00	2.50	0.097
Composite Score	1.00	5.30	0.011

[#] Accounting for clustering by school and class

[*] Effective DF closer to one suggests closer to linearity.

[**] The p-value tests the significance of the smooth term in the regression model of test score