

# Low-Level Lead Exposure and Behavior in Early Childhood

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**ABSTRACT.** *Objective.* To assess whether small elevations in blood lead level were associated with measurable behavioral changes in a group of poor children between 1 and 3 years old.

*Methods.* The study population consisted of children presenting for routine well-child care to the pediatric clinic at Bellevue Hospital Center, a large urban public hospital. The following inclusion criteria were used for entry into the study: age 12 to 36 months; capillary lead screening result  $<1.21 \mu\text{mol/L}$  ( $25 \mu\text{g/dL}$ ); no known prior history either of blood lead level  $>1.21 \mu\text{mol/L}$  ( $25 \mu\text{g/dL}$ ) or lead exposure requiring chelation therapy; Latino or African-American; English or Spanish spoken in the home; biological mother as primary caretaker; child not presently attending day care; full-term, singleton gestation; birth weight at least 2500 g; no known neurologic or developmental disorder; and no severe chronic disease, including human immunodeficiency virus infection. Study enrollment was simultaneously stratified by capillary lead level and age.

All children between 12 and 36 months attending the pediatric clinic during the study period received screening capillary blood measures of lead level following the recommendations of the Centers for Disease Control and Prevention and the American Academy of Pediatrics as part of routine primary care. During periods of enrollment, consecutive lead measurements performed in the pediatric clinic were reviewed by one of the researchers. For those children meeting entry criteria based on lead level and age, further eligibility based on the remainder of the inclusion criteria was determined through parental interview and review of the medical record.

Lead exposure was assessed with a single capillary blood specimen, using atomic absorption spectrophotometry. Subjects were considered to be lead-exposed if their lead level was between 0.48 and  $1.20 \mu\text{mol/L}$  (10 and  $24.9 \mu\text{g/dL}$ ) and nonexposed if their lead level was between 0 and  $0.48 \mu\text{mol/L}$  (0 and  $9.9 \mu\text{g/dL}$ ).

Behavior was assessed using the Behavior Rating Scale (BRS) of the *Bayley Scales of Infant Development*, second edition. The BRS in this age group consists of three components: an Emotional Regulation Factor that measures hyperactive/distractible/easy-frustration behaviors; an Orientation-Engagement Factor that measures fear/withdrawal/disinterest behaviors; and a Motor Quality Factor that assesses the appropriateness of movement

and tone. The BRS is scored as a percentile; lower scores reflect more problematic behaviors. Researchers performing the BRS were blinded to capillary lead results.

Information was collected concerning factors that might confound the relationship between lead and behavior. Demographic factors were collected, including: child's age, gender, and country of origin; mother's age, marital status, parity, country of origin, and primary language spoken; parental education, and occupation and receipt of public assistance. Socioeconomic status was determined using the *Hollingshead Two-Factor Index of Social Position*. Maternal verbal IQ was assessed using the *Peabody Picture Vocabulary Test-Revised*. Maternal depression was assessed using the Center for Epidemiologic Studies-Depression Scale. Cognitive stimulation provided in the home was assessed using a new office-based instrument, the StimQ, which measures the quantity and quality of play materials and parent-toddler activities in the child's home. To assess the child for iron deficiency, we performed a hematocrit and mean corpuscular volume at the time of the capillary lead evaluation. A presumptive diagnosis of iron deficiency was made if the child was either anemic (defined as a hematocrit  $<32$ ) or had a mean corpuscular volume  $<72$ .

*Results.* The study sample consisted of 72 children. Children in the lead-exposed group ( $n = 41$ ) had a mean BRS behavior score that was 15.8 points lower than that of children in the nonexposed group ( $n = 31$ ), which was significant by the Student's *t* test. For the emotional regulation factor measuring hyperactive/impulsive/easy-frustration behaviors, children in the exposed group had a mean score that was 14.6 points lower than that of the nonexposed group, which was significant by the Student's *t* test. For the orientation-engagement factor measuring fear/withdrawal/disinterest behaviors, children in the exposed group had a mean score that was 14.1 points lower, significant by the Student's *t* test.

Multiple linear regression analyses were used to examine the independent relationship between BRS (total and factor scores) and lead group, after adjusting for potential confounders. Six variables were related to either lead group or BRS behavior score in unadjusted analysis and were, therefore, included as potential confounders in each of the multiple regressions: child's age and gender, and mother's age, verbal IQ, depression score, and provision of cognitive stimulation.

In the analysis of the relationship between the BRS total score and lead group, the adjusted mean BRS behavior score in the exposed group was 17.3 points (95% confidence [CI]: 3.3, 31.3) lower than that of children in the nonexposed group ( $sr = -0.27$ ). In the analysis of the relationship between the emotional regulation factor and lead group, the adjusted mean factor score in the exposed group was 16.6 points (95% CI: 2.1, 31.2) lower than that for the nonexposed group ( $sr = -0.25$ ). In the analysis of the relationship between the orientation-engagement factor and lead group, the exposed group had an adjusted

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mean score that was 14.2 points (95% CI: -2.1, 30.5) lower than that for the nonexposed group ( $sr = -0.20$ ).

In these multiple regression analyses, mother's depression score was significantly associated with a lower total BRS score ( $sr = -0.25$ ) and with lower emotional regulation factor ( $sr = -0.23$ ). Older children had higher BRS scores ( $sr = 0.20$ ), and had significantly higher emotional regulation factor scores ( $sr = 0.22$ ). A relationship was observed between male gender and lower emotional regulation scores that did not reach significance ( $sr = -0.21$ ). Iron deficiency, cognitive stimulation provided in the home and mother's verbal IQ were not related to any measures of behavior.

**Conclusions.** Low-level lead exposure is associated with adverse behavioral changes in very young preschool children. This association may be particularly important for poor children, who are also at risk for behavior problems on the basis of other environmental factors such as maternal depression. Clinicians should consider screening for behavioral problems in very young children with low-level lead exposure. *Pediatrics* 1998;101(3). URL: <http://www.pediatrics.org/cgi/content/full/101/3/e10>; preschool children, lead, behavior.

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ABBREVIATIONS. BRS, Behavior Rating Scale; PPVT-R, Peabody Picture Vocabulary Test-Revised; CES-D, Center for Epidemiologic Studies-Depression Scale; CI, confidence interval; SD, standard deviation; B, unstandardized regression coefficient; sr, semi-partial correlation coefficient.

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A large body of evidence has been compiled concerning the relationship between lead exposure and behavioral problems in children. In school-aged children, problems found in association with lead exposure have included both hyperactive/impulsive/easy-frustration behaviors as well as fear/withdrawal/disinterest behaviors.<sup>1-9</sup> In early childhood, however, the ramifications remain incompletely understood. Although a few studies performed in early childhood have shown some evidence that elevations in blood lead level may be associated with behavioral changes,<sup>10,11</sup> others have not been able to confirm these findings<sup>12-15</sup>. Furthermore, it is not known whether any adverse behavioral effects result from blood lead levels  $<1.21 \mu\text{mol/L}$  ( $25 \mu\text{g/dL}$ ). In fact, in the only study to our knowledge that showed consistent relationships between blood lead level and behavior in very young children,<sup>11</sup> the mean lead level in the exposed group was  $1.35 \mu\text{mol/L}$  ( $28 \mu\text{g/dL}$ ).

As part of a study of the effects of lead exposure on early child development, we examined whether small elevations in blood lead level were associated with measurable behavioral changes in a group of poor children between 1 and 3 years old. Analysis of the relationship between blood lead level and cognitive and motor development will be reported on separately.

## MATERIALS AND METHODS

### Subjects

The study population consisted of children presenting for routine well-child care to the pediatric clinic at Bellevue Hospital Center (New York, NY), a large urban public hospital. The study was approved by the New York University School of Medicine

Institutional Board of Research Associates. Informed consent was obtained from all participating families.

The following inclusion criteria were used for entry into the study: age 12 to 36 months; capillary lead screening result  $<1.21 \mu\text{mol/L}$  ( $25 \mu\text{g/dL}$ ); no known prior history either of blood lead level  $>1.21 \mu\text{mol/L}$  ( $25 \mu\text{g/dL}$ ) or lead exposure requiring chelation therapy; Latino or African-American; English or Spanish spoken in the home; biological mother as primary caretaker; child not presently attending day care; full-term, singleton gestation; birth weight at least 2500 g; no known developmental delay; no known neurologic disorder; and no severe chronic disease, including human immunodeficiency virus infection. Although our clinic population comprises a large number of ethnic groups, Latinos and African-Americans together make up  $>85\%$  of the children. Although children of many other ethnicities receive care at our clinic, the number of children in any one of these ethnic groups is small. We were therefore concerned that we would not be able to control for cultural differences that might confound our results, and decided to exclude children whose ethnicities were other than Latino or African-American. Likewise, children in day care were excluded because of the small numbers of such patients in our population, and our resultant inability to control for the effects of day care attendance on child behavior.

A power analysis was performed to determine an appropriate sample size. To find a correlation of 0.30 with a power of 80% and a level of type I error of .05 (two-tailed), 85 subjects would be needed. Planned enrollment therefore preceded to meet this target.

The study took place between July 1993 and March 1995. All children between 12 and 36 months attending the pediatric clinic received screening capillary blood measures of lead level following the Centers for Disease Control<sup>16</sup> and American Academy of Pediatrics<sup>17</sup> recommendations as part of routine primary care. During periods of enrollment (determined by staff availability), consecutive lead measurements performed in the pediatric clinic were reviewed by one of the researchers. For those children meeting entry criteria based on lead level and age (see stratification process, below), further eligibility based on the remainder of the inclusion criteria was determined through parental interview and review of the medical record. By the end of the study, 158 children had been identified as potentially eligible for the study based on lead level and age. Of these, 50 were excluded for the following reasons: prematurity/low birth weight (9 children), known developmental delay (10), chronic illness (7), twin (3), sibling in study (1), natural mother not primary caretaker (10), attendance in day care (3), and ethnicity not Latino or African-American (7). Therefore, 108 patients were identified as eligible for the study. Of these, 18 families (16.7%) refused to participate. We were unable to locate an additional 18 families (16.7%). Although our goal had been the enrollment of 85 families, we stopped at 72 patients because of lack of institutional resources to continue the study.

The 72 children who completed the study were compared with the 36 who were eligible but did not enroll in the study because of either refusal or our inability to locate them. Information was available in both of these groups concerning age, sex, and capillary lead level; no significant differences were found.

### Assessment of Lead Exposure

Lead exposure was measured by a single capillary blood specimen, obtained by a trained technician. Blood lead levels were measured by atomic absorption spectrophotometry (Hitachi Z-9000; Danbury, CT). Quality control was assessed by comparing paired capillary and venous specimens (obtained within 2 weeks of each other) in a subsample of 17 children; Pearson's correlation coefficient was 0.94,  $P < .001$ . On average, capillary lead levels were slightly higher than venous lead levels; the mean difference was  $0.09 \mu\text{mol/L}$  ( $1.9 \mu\text{g/dL}$ ); standard deviation was  $0.15 \mu\text{mol/L}$  ( $3.5 \mu\text{g/dL}$ ).

### Stratification Process

To generate a sample of children with a balanced distribution of lead levels across the range being studied, enrollment was stratified by capillary lead level into two categories:  $0-0.48 \mu\text{mol/L}$  ( $0-9.9 \mu\text{g/dL}$ ) and  $0.48-1.20 \mu\text{mol/L}$  ( $10-24.9 \mu\text{g/dL}$ ). However, after the enrollment process had begun, it became clear that because of the skewed distribution of leads in our clinic, most of the enrolled children had lead levels closer to the lower end of their

stratification ranges (ie, children in the 0–0.48  $\mu\text{mol/L}$  [0–9.9  $\mu\text{g/dL}$ ] group primarily had leads <0.24  $\mu\text{mol/L}$  [5  $\mu\text{g/dL}$ ], and children in the 0.48–1.20  $\mu\text{mol/L}$  [10–24.9  $\mu\text{g/dL}$ ] group had leads <0.72  $\mu\text{mol/L}$  [15  $\mu\text{g/dL}$ ]). In addition, the children with lead levels between 0.48–1.20  $\mu\text{mol/L}$  (10–24.9  $\mu\text{g/dL}$ ) tended to be younger than the children with lower lead levels, which could have caused age to be a confounder in the analysis. To correct this problem, the enrollment process was modified in the following way: entry into the study was stratified simultaneously by both capillary lead level and age. Capillary lead level was stratified into four categories: 0–0.24, 0.24–0.48, 0.48–0.72 and 0.72–1.20  $\mu\text{mol/L}$  (0–4.9, 5.0–9.9, 10.0–14.9, and 15.0–24.9  $\mu\text{g/dL}$ ); age was also stratified into 4 categories: 12–17.9, 18–23.9, 24–29.9 and 30–35.9 months. Entry into the study then continued for children whose combinations of lead and age had been under-represented during the initial process.

### Assessment of Potential Confounders

Information was collected concerning demographic, home environmental and medical factors that might influence behavior.

Demographic factors were collected by parent interview, and included: child's age, gender, and country of origin; mother's age, marital status, parity, country of origin, and primary language spoken; parental education and occupation and receipt of public assistance. Socioeconomic status was determined using the *Hollingshead Two-Factor Index of Social Position*,<sup>18</sup> based on parental education and occupation.

Information was collected about other factors related to behavior and development including maternal verbal IQ, maternal depression, and a measure of cognitive stimulation provided in the home. Maternal verbal IQ was assessed using the *Peabody Picture Vocabulary Test-Revised* (PPVT-R)<sup>19</sup> Maternal depression was assessed using the Center for Epidemiologic Studies-Depression Scale (CES-D), an interviewer-administered questionnaire.<sup>20</sup> Both the PPVT-R and the CES-D are standardized for use in both English- and Spanish-speaking populations. Cognitive stimulation provided in the home was assessed using a new office-based instrument, the StimQ,<sup>21</sup> which measures the quantity and quality of play materials and parent-toddler activities in the child's home. All interviews and tests were performed in the primary language of the family.

There are many medical factors that can affect developmental outcome, such as prematurity and human immunodeficiency virus infection. Our study enrollment criteria (see above) excluded children with some of these problems. One additional problem commonly seen in our population that may confound the relationship between lead and behavior is iron deficiency.<sup>10,22</sup> To assess the child for iron deficiency, we performed a hematocrit and mean corpuscular volume at the time of the capillary lead evaluation. A presumptive diagnosis of iron deficiency was made if the child was either anemic (defined as a hematocrit <32) or had a mean corpuscular volume <72.<sup>23</sup>

### Assessment of Behavior

Behavior was assessed using the Behavior Rating Scale (BRS) of the *Bayley Scales of Infant Development*, second edition.<sup>24</sup> The scale on which the BRS is based, the Infant Behavior Record of the original *Bayley Scales*,<sup>25</sup> has been used frequently as an outcome measure in studies of child development.<sup>12,15,22,26</sup> Reliability studies of the revised BRS have shown excellent internal consistency and good to excellent test-retest stability and inter-rater agreement.<sup>24</sup>

The BRS behavior scale was performed by one of seven trained Bayley administrators, who observed the child's behavior while the child performed the tasks required of the *Bayley Scales*. When two administrators were available, they each scored the BRS and reached a consensus to determine a final score. As part of the BRS, each parent was queried as to whether the behavior observed during the test was typical of what occurred in the home.

To achieve reliability, each Bayley administrator attended a formal training program sponsored by the publishers of the scale. Before performing the Bayley independently, each Bayley administrator first observed the performance of at least five Bayley examinations and then performed five Bayleys under the direct supervision of one of the principal investigators (A.L.M. and B.P.D.). To maintain reliability, these two investigators periodically observed administrations of the Bayley scales and provided feedback as appropriate.

The BRS in this age group consists of three components: an Emotional Regulation Factor that measures hyperactive/distractible/easy-frustration behaviors; an Orientation-Engagement Factor that measures fear/withdrawal/disinterest behaviors; and a Motor Quality Factor that assesses the appropriateness of movement and tone. The BRS is scored as a percentile; lower scores reflect more problematic behaviors. Percentile scores are classified into three categories: normal,<sup>26–99</sup> questionable,<sup>11–25</sup> and nonoptimal.<sup>1–10</sup> Researchers performing the Bayley BRS were blinded to capillary lead results.

### Statistical Analysis

Data were analyzed using SPSS (SPSS, Inc, Chicago, IL), version 6.1.<sup>27</sup> A two-tailed *P* value <.05 was considered to be statistically significant.

$\chi^2$  analysis and two sample Student's *t* tests were used to compare participants in the study to eligible nonparticipants with respect to age, sex, and lead level.

Because the Centers for Disease Control<sup>16</sup> and the American Academy of Pediatrics<sup>17</sup> define a lead level >0.48  $\mu\text{mol/L}$  (10  $\mu\text{g/dL}$ ) as high enough to warrant intervention, and because 1.21  $\mu\text{mol/L}$  (25  $\mu\text{g/dL}$ ) has typically represented the lower bound for moderate lead exposure, subjects were divided into two groups: low-level lead-exposed (defined as lead between 0.48 and 1.20  $\mu\text{mol/L}$  [10 and 24.9  $\mu\text{g/dL}$ ]) and nonexposed (defined as lead between 0 and 0.48  $\mu\text{mol/L}$  [0 and 9.9  $\mu\text{g/dL}$ ]). Two sample Student's *t* tests were used to compare BRS scores and factors between the exposed and nonexposed groups. Multiple linear regression analyses were then used to determine the independent associations between lead exposure and measures of behavior after adjusting for confounders.<sup>28</sup> In these regressions, BRS total score, Emotional Regulation Factor score, Orientation-Engagement Factor score, and Motor Factor score were the dependent variables. Predictor variables consisted of lead group (dummy coded so that exposed children were coded 1 and nonexposed children were coded 0) and a set of potential confounders. All possible covariates were considered for entry into the model, including child's age, sex, country of origin (US-born vs not), and presence of iron deficiency, mother's age, marital status (married vs not), education (high school graduate vs not), parity, verbal IQ (PPVT-R), depression score (CES-D), and provision of cognitive stimulation in the home (StimQ); and family ethnicity, principal language spoken in the home (Spanish or bilingual vs English), Hollingshead Index of Social Position Score, and receipt of public assistance. However, each covariate was entered into the multiple regression model only if the *P* value for its simple relationship with either lead group or BRS score was <.10 (analyzed by *t* test, analysis of variance, Pearson correlation, or  $\chi^2$  as appropriate). Also, each covariate used in the regression analyses was assessed for the possibility of an interaction with lead group.

In addition, the relationship between lead and behavior was analyzed using lead as a continuous variable. Simple correlations between lead level and BRS total score and subscores were obtained. Multiple regression analyses were performed in an analogous manner to the multiple regressions that had been performed with lead considered in a dichotomous manner.

$\chi^2$  analysis was used to compare categorical scores on the BRS (normal vs questionable or nonoptimal) between exposed and nonexposed children. Multiple logistic regression analysis was used to determine the association between lead group and categorical behavior score after adjusting for confounders (consisting of the same variable set used in the multiple linear regression analysis).

## RESULTS

### Study Participant Characteristics

Descriptive data for the 72 families who comprised the study sample are presented in Table 1. The majority of families were of Latino origin, spoke Spanish as their primary language, and had low socioeconomic status (Hollingshead classes IV and V). Many mothers were depressed (defined by a CES-D score of 16 or more). Few children were iron-deficient.

The joint frequency distribution of lead level by

**TABLE 1.** Characteristics of Study Sample\*

	Total Sample (n = 72)	Exposed† (n = 41)	Nonexposed‡ (n = 31)	P§
Lead level, $\mu\text{mol/L}$	0.50 (0.24)	0.70 (0.19)	0.23 (0.12)	NA
Demographic factors				
Child				
Age, mo	22.9 (6.6)	22.3 (6.5)	23.8 (6.7)	.34
Female	45.8%	56.1%	32.3%	.07
Born in United States	86.1%	80.5%	93.5%	.21
Mother				
Age, y	26.3 (5.0)	25.2 (4.3)	28.0 (5.5)	.02
Married	76.4%	78.0%	74.1%	.91
Parity	2.2 (1.2)	2.1 (1.2)	2.3 (1.2)	.61
HS grad	54.2%	46.3%	64.5%	.20
Born in United States	23.6%	22.0%	25.8%	.91
Family				
Ethnicity				.80
Latino	95.8%	97.6%	93.5%	
African American	4.2%	2.4%	6.5%	
Primary language				.17
English	15.3%	14.9%	16.1%	
Spanish	62.5%	70.7%	51.6%	
Bilingual	22.2%	14.6%	32.3%	
Hollingshead SES				.28
SES 1-3	5.6%	7.3%	3.2%	
SES 4	27.8%	26.8%	29.0%	
SES 5	66.7%	65.9%	67.7%	
Public assistance	47.2%	39.0%	58.1%	.17
Home environment				
Cognitive, StimQ¶	12.5 (4.9)	11.7 (5.1)	13.6 (4.3)	.09
Mother depressed	41.7%	43.9%	38.7%	.84
Maternal IQ, PPVT	84.8 (22.5)	80.0 (19.8)	91.1 (24.6)	.04
Medical				
Iron-deficient	13.9%	9.8%	19.4%	.41

\* Data are presented as mean (SD) or percent.

† Lead level between 0.48 and 1.20  $\mu\text{mol/L}$  (10 and 24.9  $\mu\text{g/dL}$ ).

‡ Lead level between 0 and 0.48  $\mu\text{mol/L}$  (0 and 9.9  $\mu\text{g/dL}$ ).

§ P value for comparison between exposed and nonexposed groups based on t test or  $\chi^2$  as appropriate.

|| NA = not applicable.

¶ Expected mean  $\pm$  SD for StimQ in low SES population: 14.2  $\pm$  5.1.<sup>21</sup>

age is shown in Table 2. The final sample was more balanced with respect to these variables than it would have been in the absence of our stratification process.

A total of 92% of parents stated that the behavior that had been observed in the clinic was typical of what occurred in the home.

**Lead and Behavior**

Children in the lead-exposed group had a mean BRS behavior score that was 15.8 points lower than that of children in the nonexposed group, which was significant by the Student’s t test at P = .02 (Table 3). For the emotional regulation factor measuring hyperactive/impulsive/easy-frustration behaviors,

**TABLE 2.** Joint Frequency Distribution of Study Sample for Lead Level by Age\*

Age, mo	Lead Level, $\mu\text{mol/L}$				Total
	0–0.24	0.24–0.48	0.48–0.72	0.72–1.20	
12–17.9	4	4	6	6	24
18–23.9	4	4	8	3	19
24–29.9	3	3	8	3	17
30–35.9	6	3	4	3	16
Total	17	14	26	15	72

\* Data are presented as number of children having each combination of lead level and age.

**TABLE 3.** Simple Comparisons of Behavior Rating Scale Total and Factor Scores by Lead Group\*

	Exposed† (n = 41)	Nonexposed‡ (n = 31)	P§
BRS total score (percentile)	46.9 (29.5)	62.7 (26.1)	.02
Emotional Regulation Factor	40.8 (29.5)	55.4 (29.8)	.04
Orientation Engagement Factor	45.1 (33.8)	59.2 (27.9)	.06
Motor Factor	91.3 (19.8)	93.0 (18.0)	.71

\* Data are presented as mean (SD).

† Lead level between 0.48 and 1.20  $\mu\text{mol/L}$  (10 and 24.9  $\mu\text{g/dL}$ ).

‡ Lead level between 0 and 0.48  $\mu\text{mol/L}$  (0 and 9.9  $\mu\text{g/dL}$ ).

§ P value based on t test.

children in the exposed group had a mean score that was 14.6 points lower than that of the nonexposed group, which was significant by the Student’s t test at P = .04. For the orientation-engagement factor measuring fear/withdrawal/disinterest behaviors, children in the exposed group had a mean score that was 14.1 points lower, with P = .06 by the Student’s t test. No relationship was observed between lead and the motor quality factor.

Multiple linear regression analyses were used to examine the independent relationship between BRS (total and factor scores) and lead group, after adjusting for potential confounders. A variable was considered to be a potential confounder if it were related to either lead group or BRS behavior score in unad-

justed analysis with  $P < .10$ . As shown in Table 1, four variables that met this criterion with their relationship to lead exposure: child's sex, mother's age, mother's verbal IQ, and provision of cognitive support in the home. In addition, two variables met this criterion with their relationship to BRS behavior score: child's age ( $r = 0.26$ ,  $P = .03$ ) and mother's depression score ( $r = -0.22$ ,  $P = .07$ ). Therefore, six variables were included as potential confounders in each of the multiple regressions: child's age and gender, and mother's age, verbal IQ, depression score, and provision of cognitive stimulation.

In the analysis of the relationship between the BRS total score and lead group (Table 4), the adjusted mean BRS behavior score in the exposed group was 17.3 points (95%CI: 3.3, 31.3) lower than that of children in the nonexposed group ( $sr = -0.27$ ,  $P = .02$ ).

In the analysis of the relationship between the emotional regulation factor and lead group (Table 5), the adjusted mean factor score in the exposed group was 16.6 points (95%CI: 2.1, 31.2) lower than that for the nonexposed group ( $sr = -0.25$ ,  $P = .03$ ).

In the analysis of the relationship between the orientation-engagement factor and lead group (Table 6), the exposed group had an adjusted mean score that was 14.2 (95% CI: -2.1, 30.5) points lower than that for the nonexposed group ( $sr = -0.20$ ,  $P = .09$ ).

No interactions were found between lead and any other variable.

When BRS results were considered in a categorical fashion, 29% of children in the lead exposed group had BRS scores that were either questionable (11th–25th percentile) or nonoptimal (1st–10th percentile), compared with 13% in the nonexposed group. Although the difference was not statistically significant ( $P = .17$ ), the power to find significance was only 0.48. In a multiple logistic regression analysis that included the same set of six potential confounders, the adjusted odds ratio for having a questionable or nonoptimal score in the exposed group was 3.9 (95% CI 0.9, 17.3;  $P = .07$ ).

When the relationship between lead and behavior was analyzed with lead as a continuous variable, the correlation was negative but nonsignificant ( $r = -0.18$ ,  $P = .11$ ). In a multiple regression with lead analyzed as a continuous variable and controlling for the same set of six potential confounders, a nonsignificant relationship was observed between lead and total BRS score ( $B = 1.1$ ,  $sr = -0.20$ ,  $P = .08$ ; overall  $F = 2.1$ ,  $P = .06$ ). In a multiple logistic regression

**TABLE 4.** Multiple Regression Results for Behavior Rating Scale Total Score\*

Independent Variable	B	sr†	P
Child's age (mo)	1.0	0.20	.07
Male gender	-8.6	-0.14	.22
Cognitive stimulation	0.3	0.04	.74
Mother's age (y)	-0.5	-0.08	.49
Mother's verbal IQ	-0.1	-0.06	.57
Mother's depression score	-0.8	-0.25	.03
Child lead-exposed‡	-17.3	-0.27	.02

\* Overall regression:  $F = 2.6$ ;  $P = .02$ .

† sr, Semipartial correlation coefficient.

‡ Lead level between 0.48 and 1.20  $\mu\text{mol/L}$  (10 and 24.9  $\mu\text{g/dL}$ ).

**TABLE 5.** Multiple Regression Results for Emotional Regulation Factor Score\*

Independent Variable	B	sr	P
Child's age (mo)	1.1	0.22	.04
Male gender	-14.0	-0.21	.06
Cognitive stimulation	-0.1	-0.02	.89
Mother's age	-0.1	-0.22	.84
Mother's verbal IQ	-0.1	-0.05	.66
Mother's depression score	-0.8	-0.23	.04
Child lead-exposed†	-16.6	-0.25	.03

\* Overall regression:  $F = 2.8$ ;  $P = .01$ .

† Lead level between 0.48 and 1.20  $\mu\text{mol/L}$  (10 and 24.9  $\mu\text{g/dL}$ ).

**TABLE 6.** Multiple Regression Results for Orientation Engagement Factor Score\*

Independent Variable	B	sr	P
Child's age (mo)	0.2	0.16	.16
Male gender	-7.3	-0.11	.37
Cognitive stimulation	-0.4	-0.05	.64
Mother's age	-0.1	-0.02	.87
Mother's verbal IQ	0.1	0.04	.73
Mother's depression score	-0.7	-0.20	.10
Child lead-exposed†	-14.2	-0.20	.09

\* Overall regression:  $F = 1.4$ ;  $P = .24$ .

† Lead level between 0.48 and 1.20  $\mu\text{mol/L}$  (10 and 24.9  $\mu\text{g/dL}$ ).

analysis with lead analyzed as a continuous variable and BRS considered categorically, the adjusted odds ratio for having a questionable or nonoptimal score in the exposed group was 1.1 for each 0.05  $\mu\text{mol/L}$  (1  $\mu\text{g/dL}$ ) increase in lead level ( $P = .13$ ).

#### Covariates/Confounders and Behavior

In multiple regression analyses (see Tables 4 and 5), mother's depression score was significantly associated with lower total BRS score ( $sr = -0.25$ ,  $P = .03$ ) and with lower emotional regulation factor ( $sr = -0.23$ ,  $P = .04$ ). Older children had higher BRS scores ( $sr = 0.20$ ,  $P = .07$ ), and had significantly higher emotional regulation factor scores ( $sr = 0.22$ ,  $P = .04$ ). A nonsignificant relationship was observed between male gender and lower emotional regulation scores ( $sr = -0.21$ ,  $P = .06$ ). Iron deficiency, cognitive stimulation provided in the home, and mother's verbal IQ were not related to any measures of behavior.

#### DISCUSSION

In this study of very young children, we were able to document a statistically significant association between postnatal lead levels in the range of 0.48 to 1.20  $\mu\text{mol/L}$  (10–24.9  $\mu\text{g/dL}$ ) and increased hyperactivity, distractibility and low frustration tolerance, and a trend toward a similar association with increased fearfulness, social withdrawal and disinterest in surroundings. These associations persisted after controlling for potential confounders, including child's age and gender, and mother's age, verbal IQ, depression score, and provision of cognitive stimulation. Although we did not show a statistically significant relationship between behavior and lead considered in a continuous manner, it is possible that this was a power issue, because we did not succeed in enrolling our entire planned sample of 85 children.

To our knowledge, these findings have not previously been reported at such a young age with low-level lead exposure. The association between lead exposure and behavior is particularly important to consider in poor children, whose behavior may be adversely affected on the basis of other environmental factors.

Previous studies have yielded conflicting results. In a study by Sciarillo<sup>11</sup> of 2- to 5-year-old African-American children in Baltimore, children with an average lead of 1.35  $\mu\text{mol/L}$  (28  $\mu\text{g/dL}$ ) had an increase in both hyperactive/impulsive and fear/withdrawal behaviors when compared with children with an average lead of 0.43  $\mu\text{mol/L}$  (9  $\mu\text{g/dL}$ ). In contrast, in a study of 2- to 5-year-old Latino children in Los Angeles with lead levels between 0.14 and 1.30  $\mu\text{mol/L}$  (3 and 27  $\mu\text{g/dL}$ ), Johnson<sup>10</sup> showed an association between lead level and aggressive behavior in only one subgroup (4- to 5-year-old girls). However, no association was found in the overall group or in any other subgroup. Furthermore, Wolf<sup>15</sup> found no relationship between lead level obtained from 1- to 2-year-old Costa Rican children (range 0.24–1.79  $\mu\text{mol/L}$  (5–37  $\mu\text{g/dL}$ )) and measures of behavior at 5 years. Finally, in a prospective study performed in Cincinnati, Dietrich<sup>12</sup> showed no association with either hyperactive/impulsive or fear/withdrawal behavior in 2-year-olds with mean lifetime blood leads <0.97  $\mu\text{mol/L}$  (20  $\mu\text{g/dL}$ ). Given these conflicting results, additional research would be useful in confirming the findings of our study.

There were several strengths in our study design that may have enabled us to find significant results. For example, the study sample was socially homogeneous and relatively free of confounding medical factors. Also, in using our stratification process, we guaranteed sufficient numbers of children with a wide range of lead level in both the exposed and nonexposed groups. These strategies, also used in studies of the effects of lead exposure in school-aged children,<sup>29,30</sup> may have enabled us to show a significant association even with a relatively small sample size.

The clinical importance of the behaviors observed in association with elevated blood lead level depends in part on the degree to which they in fact reflect adverse behavioral changes seen in other settings and in part on whether they predict later outcomes related to behavior. Rapoport,<sup>31</sup> in a study of hyperactive children, found a high correlation between behavior observed by professionals in a clinic and behavior observed by parents in the home. In our study, the great majority of mothers considered the behavior seen to be typical. Furthermore, we do not know whether the behaviors that we observed will persist as that child gets older. Egeland<sup>32</sup> found that 71% of withdrawn preschoolers and 80% of acting-out preschoolers had persistence of these problems in first or second grade; however, his sample differed from ours in that he studied somewhat older children who were considered to be at high risk for persistent behavioral problems on the basis of caregiver issues. Finally, we do not know whether the magnitude of the behavior changes observed in this

study will have clinical significance for the child and family. Longitudinal follow-up through school age of a study cohort such as our own would help to determine whether the types of adverse behaviors reported in this study persist and whether they are associated with later problems involving school functioning or social adaptation.

Interestingly, the children in the nonexposed group scored somewhat better than would have been expected from a random sample of the population; similarly, fewer scored in the questionable or nonoptimal range. We speculate that one cause might have been our selection process, in which we preselected children who were neurologically normal and had no known developmental delays. Therefore, our patients had higher than average scores on the motor component of the behavior scale (see Table 3).

One limitation of our study was the use of a single blood sample as our measure of lead burden. Studies that have observed the stability of lead levels over time have yielded conflicting evidence. Ernhart<sup>33</sup> and Cooney<sup>34</sup> each found an intercorrelation among consecutive lead levels performed in the first 4 years of life to be between 0.4 and 0.75. Rabinowitz<sup>35</sup> found an intercorrelation between 0.1 and 0.6 in the first 12 to 24 months, with between 38% and 55% remaining in a given lead exposure category during any 6-month interval. Furthermore, as pointed out by Rutter,<sup>36</sup> a normal level does not exclude past exposure. Using serial measures of lead exposure would have strengthened any results that were found. However, had our single blood sample not been reflective of past exposure, we would have expected that this would have tended to make the lead exposed and nonexposed groups less different; the fact that we found behavioral changes in the exposed group suggests that our measure of lead was meaningful.

Consistent with other studies,<sup>11,37</sup> maternal depression was adversely related to behavior. Given its high prevalence, depression may play an important role in preschool behavior problems in our population. In contrast to some other studies,<sup>10,22</sup> possible iron deficiency was not related to behavior. However, given the small number of iron-deficient children in our sample, there may not have been sufficient power to show an effect.

## CONCLUSION

In summary, the early morbidity of low-level lead exposure may include behavioral changes. Consideration should be given to screening for behavioral problems in young children with low-level lead exposure. Clinicians should continue in their efforts in the prevention of the exposure of young children to environmental lead.

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