



# Prenatal Lead Exposure Modifies the Impact of Maternal Self-Esteem on Children's Inattention Behavior

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**Objective** To prospectively evaluate the association of maternal self-esteem measured when their offspring were toddlers with the subsequent development of attention deficit hyperactivity disorder (ADHD)-like behavior in their school-age offspring and the potential modifying effects of prenatal lead exposure.

**Study design** We evaluated a subsample of 192 mother-child pairs from a long-running birth-cohort project that enrolled mothers in Mexico from 1994-2011. Prenatal lead exposure was assessed using cord blood lead and maternal bone lead around delivery (tibia and patella lead, measured by K-x-ray-fluorescence). When children were 2 years old, maternal self-esteem was measured using the Coopersmith Self-Esteem Inventory. When children were 7-15 years old, children's blood lead levels and ADHD symptoms were assessed, and Conners' Parent Rating Scale-Revised and Behavior Rating Inventory of Executive Function-Parent Form were used as measures of ADHD-like behavior.

**Results** Adjusting for family economic status, marital status, maternal education and age, child's age and sex, and children's current blood lead levels, increased maternal self-esteem was associated with reduced child inattention behavior. Compared with those among high prenatal lead exposure (P25-P100), this association was stronger among low prenatal lead exposure groups (P1-P25, *P* values for the interaction effects between prenatal lead exposure and maternal self-esteem levels of  $<.10$ ). Each 1-point increase in maternal self-esteem scores was associated with 0.6- to 1.3-point decrease in Conners' Parent Rating Scale-Revised and Behavior Rating Inventory of Executive Function-Parent Form T-scores among groups with low cord blood lead and patella lead (P1-P25).

**Conclusions** Children experiencing high maternal self-esteem during toddlerhood were less likely to develop inattention behavior at school age. Prenatal lead exposure may play a role in attenuating this protective effect. (*J Pediatr* 2015;167:435-41).

Compared with single exposure studies, mixed exposures of neurotoxic chemicals and social context may better reflect real-world exposure scenarios and, therefore, are of particular importance.<sup>1-3</sup> The potential effects of the interaction between the neurotoxic chemicals and social environment on children's neurodevelopment has been previously suggested in animal studies,<sup>4</sup> but few studies have focused on such interaction effects in human populations.

Attention deficit hyperactivity disorder (ADHD) affects around 5% of school-age children,<sup>5</sup> with the potential to persist into adulthood. A growing body of evidence suggests that early-life lead exposure, even at very low levels of exposure (ie, children's blood lead levels below 5  $\mu\text{g}/\text{dL}$ ), is a potential contributor to ADHD.<sup>2,6-8</sup>

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ADHD	Attention deficit hyperactivity disorder
BRIEF	Behavior Rating Inventory of Executive Function
CPRS-R	Conners' Parent Rating Scale-Revised
DSM-IV	<i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i>
P-ADHD	ADHD index
P-BRI	Behavioral regulation index
P-DSMHI	DSM-IV ADHD hyperactivity/impulsivity index
P-DSMI	DSM-IV ADHD inattention index
P-DSMT	DSM-IV ADHD combined index
P-GEC	Global executive composite
P-MI	Metacognition index

Maternal self-esteem is used to reflect the overall emotional evaluation of a mother's own worth. Self-esteem and stress are closely related because high self-esteem may buffer stressors, and low self-esteem may cause a higher level of perceived stress.<sup>9</sup> Maternal low self-esteem and maternal stress may share a similar mechanism of developmental neurotoxicity.<sup>10,11</sup> Although study results are equivocal, associations between maternal stress and ADHD in children have been shown in clinical studies as well as epidemiologic studies that controlled for potential confounders.<sup>12-14</sup> However, the exact association between maternal self-esteem and her child's ADHD-like behavior is still unknown.

The epidemiologic research has shown that compared with low self-esteem, higher maternal self-esteem attenuates the negative effects of lead on children's cognitive performances.<sup>11</sup> Previous studies also showed that maternal lead exposure and stress exposure may interact such that impacts of either risk could change in the presence of the other.<sup>1,2,4</sup>

Therefore, we utilized data from a long-running birth cohort project to examine prospectively the effects of maternal self-esteem on school-age children's ADHD-like behavior and the potential modifying effects of prenatal lead exposure.

## Methods

Subjects were recruited from 3 birth cohorts in Mexico city that composed the Early Life Exposures in Mexico to Environmental Toxicants project during 1994-1997 (cohort 1), 1997-2000 (cohort 2), and 2001-2005 (cohort 3). Pregnant women with low to medium income were enrolled from 3 maternity hospitals. Cohort 1 was enrolled at the time of delivery, and cohort 2 and 3 were during pregnancy. The mother-offspring pairs were excluded if the mother or child had pathologic factors affecting child development.<sup>15-18</sup> All 3 of the cohorts used identical exclusion criteria.<sup>15-18</sup>

Maternal bone lead levels were measured in vivo within 1 month of delivery. Of 1756 mother-offspring pairs who completed a baseline assessment during recruitment (with at least 1 measurement of prenatal lead exposure including maternal bone lead or cord blood lead), 349 pairs completed an assessment of maternal self-esteem when the offspring was 2 years old. The mother-child pairs were re-interviewed to assess childhood ADHD symptoms and children's current blood lead levels when the children were 7-15 years old. Of the 349 pairs, 192 (55.0%) completed the 7- to 15-year follow-up assessment. The most common reason for the subject loss to follow-up was lack of time to undergo the assessment. The 192 mother-child pairs were not statistically different in demographic characteristics, maternal self-esteem, cord blood lead, and maternal bone lead from the 157 pairs who were not followed-up (data not shown).

Ethics approval was received from the Institutional Review Boards of the Harvard School of Public Health, National Institute of Public Health of Mexico, University of Michigan, University of Toronto, Mount Sinai School of Medicine, and

attending hospitals. Women and children old enough signed informed consent letters before enrollment.

### The Assessment of Prenatal and Current Lead Exposure

Maternal tibia and patella lead were measured in vivo using a Cd-109 K-shell radiograph fluorescence instrument (ABIOMED, Danvers, Massachusetts).<sup>18</sup> Cord blood lead levels were measured using an atomic absorption spectrometry instrument (model 3000; PerkinElmer, Chelmsford, Massachusetts). Children's current blood lead levels were measured using inductively coupled plasma mass spectrometry (Elan 6100; PerkinElmer).<sup>18</sup> No blood lead levels were below the limit of detection.

### The Assessment of Maternal Self-Esteem

The Coopersmith Self-Esteem Inventory (Spanish version, adult short form), with 25-items and good reliability and validity, was used to measure maternal self-esteem levels. The self-esteem total scores ranged from 1-25, and higher total scores indicated higher maternal self-esteem levels.<sup>11</sup>

Other covariate data including maternal age at enrollment, family economic status, years of maternal and paternal education, marital status, and the child's sex and age, were collected by questionnaire. Because the low maternal education was associated with maternal attention and hyperactivity problems, maternal education was adjusted to partially control the heritable impacts of maternal attention and hyperactivity levels on her child's ADHD-like behavior.

### The Assessment of the School-Age Child's ADHD-Like Behavior

The validated Spanish versions of Conners' Parent Rating Scale-Revised (CPRS-R) and Behavior Rating Inventory of Executive Function (BRIEF) parent form were used for the assessment.

The 27-question CPRS-R was designed to obtain the parents' reports on children's behavioral problems in children at 3-17 years old with a good test-retest reliability and internal consistency.<sup>19</sup> We specially focused on 4 scales including ADHD index (P-ADHD), *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) ADHD inattention index (P-DSMI), DSM-IV ADHD hyperactivity/impulsivity index (P-DSMHI), and DSM-IV ADHD combined indexes (P-DSMT). The P-ADHD was associated with the risk for ADHD. P-DSMI, P-DSMHI, and P-DSMT were correspondent with the DSM-IV diagnostic criteria for inattentive, hyperactivity-impulsive, and combined subtypes of ADHD, respectively.<sup>17,19</sup> The BRIEF parent form, a reliable parent-report inventory, was used to assess behavioral regulation and metacognition in children at 5-18 years old.<sup>20</sup> BRIEF parent form contained 8 clinical scales. We focused on 2 summary scales (behavioral regulation index [P-BRI] and metacognition index [P-MI]) and another scale reflecting overall functioning (global executive composite [P-GEC]).<sup>20,21</sup> T-scores of CPRS-R and BRIEF parent scales were associated with the risk of ADHD. A child with the

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