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# Prenatal lead exposure modifies the association of maternal self-esteem with child adaptive ability

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ABSTRACT

*Background:* A child's adaptive ability is important for personal career and social development. Maternal self-esteem may help shape a child's behavior. This study aims to investigate whether maternal self-esteem measured when their children were toddlers predicts their children's adaptive skills at school age, and whether prenatal lead exposure modifies such a relationship.

*Methods:* We assessed prenatal lead exposure using cord blood lead and maternal bone lead around delivery (tibia and patella lead measured *in vivo* by K-x-ray-fluorescence) among 192 mother-child pairs investigated in Mexico from 1994 to 2011. Maternal self-esteem was measured using the Coopersmith-Self-esteem-Inventory when children were 2 years old. When children were 7-to-15 years old, we measured children's blood lead levels and administered the 2nd edition of Behavior-Assessment-System-for-Children (BASC-2) parent-rating-scales (PRS) and Self-Reports of Personality (SRP) to evaluate children's adaptive skills.

*Results:* Median (P25, P75) values for maternal patella and tibia lead, cord blood lead and children's current blood lead levels were 12.6 (3.2, 21.7) μg/g, 10.2 (4.1, 16.0) μg/g, 5.5 (3.5, 8.1) μg/dL and 2.7 (2.0, 4.0) μg/dL, respectively. In adjusted models, increased maternal self-esteem was associated with increased adaptive T-scores on the BASC-2 PRS and SRP scales. This relationship was weaker in high prenatal lead-exposure groups (high cord blood lead or patella lead groups, P25—P100) compared with low prenatal lead-exposure (low cord blood lead or patella lead groups, P1—P25) groups ($P$-interaction values $< 0.10$). No significant interactions between maternal tibia lead and self-esteem on children's adaptive T-scores were observed ($P$-interaction values $> 0.10$).

*Conclusions:* Toddlers of mothers with high (*vs.* low) self-esteem have better adaptive abilities when they are of school-age. Prenatal lead exposure may attenuate or eliminate this positive association.

*Abbreviations:* the 2nd edition of Behavior-Assessment-System-for-Children: BASC-2, parent-rating-scales: PRS; Self-Reports of Personality: SRP. P-SS, the parent rating scale for social skills; P-LEA, the parent rating scale for leadership; P-ADL, the parent rating scale for activities of daily living; P-ADA, the parent rating scale for adaptability; P-FC, the parent rating scale for functional communication; SR, self-reliance

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## 1. Introduction

Maternal self-esteem, as a good indicator for maternal psychological functioning (Brand et al., 2015), may provide an essential part of early experiences that later may directly shape a child's behavior (Phelan et al., 2014; Wickham et al., 2015). While previous studies investigated maternal psychological impacts in isolation, the effects of maternal self-esteem always occur in a real-world setting with numerous risk modifiers, including environmental (such as lead) and genetic factors, which may have the potential to influence the association of maternal self-esteem (Abbott et al., 2018; Surkan et al., 2008; Tamayo et al., 2017; Xu et al., 2015). Although a potential interaction between maternal stress and prenatal lead exposure on offspring neurobehavior has been suggested in previous animal studies (Cory-Slechta et al., 2012, 2013a,b), few studies have assessed such interactions in humans (Surkan et al., 2008; Tamayo et al., 2017; Xu et al., 2015), and nothing is known about how neurotoxic chemicals (such as lead) modulate the association of maternal self-esteem with child adaptive behavior.

Adaptive ability refers to a child's social and practical competence to live independently and to function safely and appropriately in everyday life, reflects the ability to deal with unexpected changes in the environment and the ability to get along in his/her environment with greatest harmony and least conflict with others, and is closely associated with his/her future career success and personal sense of happiness (Liu and Raine, 2017; Yarnell et al., 2015). The adaptive ability can be independent of cognitive ability. Deficits in adaptive behavior can be observed in self-care skills and social relationships (Tassé et al., 2012). Children with autism-like behaviors usually had lower ratings in adaptive behavior than the general population (Volker et al., 2010). In spite of the importance of adaptive behavior for a child's future life, few studies have investigated the correlates of children's adaptive behavior.

A child's social-emotional response or competence is firmly rooted in the context of mother-child interactions beginning in early life. Early experiences, especially emotionally or affectively charged experiences with mothers, may shape children's later development of adaptive capacity (Malekpour, 2007). Previous studies have suggested that compared with mothers with low psychological functioning, mothers who responded more sensitively to children's cues and had mother-child dyadic pleasure reacted to the needs of their children in a more accurate and attuned way, and therefore facilitated more optimal behavioral/emotional development and adaptive functioning in their children (Fenning and Baker, 2012; Laor et al., 2001; Porcerelli et al., 2016). However, until now, no studies have directly assessed the association of maternal self-esteem with child adaptive behavior.

Maternal self-esteem levels are closely and inversely related to their stress levels. Low self-esteem makes women more vulnerable to stressful situations, while high self-esteem offers protection from stressful episodes and may act as a buffer against the potentially toxic effects of the neuroendocrine responses induced by stress. Both lead exposure and stress/ or low self-esteem disproportionately affect low socio-economic status populations (Veselska et al., 2010), and contribute to an increased risk of neurobehavioral disorders in the offspring (Surkan et al., 2008; Xu et al., 2015). The potential interaction between lead and maternal stress or self-esteem on neurodevelopment has been proposed based on physiological consideration and previous findings (Cory-Slechta, 2005; Surkan et al., 2008; Tamayo et al., 2017; Virgolini et al., 2008; Weston et al., 2014; Xu et al., 2015). Prenatal lead exposure due to internal or external lead exposure during pregnancy affects development of fetal brain mesocorticolimbic dopamine system, which is a key target of lead effects on behavior and has extensive interactions with the hypothalamic-pituitary-adrenal axis, the system that coordinates the body's physiological response to stress (Virgolini et al., 2008), and thus may alter the susceptibility of children to maternal stress induced by low self-esteem. In addition, although previous studies suggested the interaction between prenatal lead exposure and maternal self-esteem on offspring's cognition or inattention behavior (Surkan et al., 2008; Xu et al., 2015), the potential modifying effect of prenatal lead exposure on the relationship between maternal self-esteem and child adaptive ability has not been explored and remains unknown.

Therefore, we hypothesized that maternal self-esteem during the early stage of life would predict their children's later adaptive ability, and prenatal lead exposure may influence this effect. Hence, we investigated the association between maternal self-esteem during toddlerhood and children's adaptive behavior at school age, and the potential modifying effects of prenatal lead exposure, utilizing the data generated during the course of a long-running birth cohort project.

## 2. Methods

### 2.1. Study design and the participants

This study included mother-child pairs from three birth-cohort studies conducted in Mexico City that comprised the Early Life Exposures in Mexico to Environmental Toxicants (ELEMENT) Project. Subjects of Cohort 1, 2 and 3 were recruited during 1994–1997, 1997–2001 and 2001–2005, respectively. All three cohorts used identical inclusion and exclusion criteria. Mother-child pairs with medical conditions that may affect child development including severe complications of pregnancy, low birth weight and clinically diagnosed asphyxia of newborn were excluded (Fortenberry et al., 2014; Surkan et al., 2008; Xu et al., 2015; Zhang et al., 2012). Detailed information on the study design, participant recruitment and data collection has been shown in previous publications (Fortenberry et al., 2014; Surkan et al., 2008; Xu et al., 2015; Zhang et al., 2012).

Umbilical cord blood lead was analyzed, and maternal bone lead was assessed *in vivo* within a month of delivery. Among the 2984 women who were recruited, 1756 women were assessed for prenatal lead exposure levels (with at least 1 measurement of prenatal lead exposure including umbilical cord blood lead or maternal bone lead), and a subgroup of 349 eligible mother-child pairs completed the assessment of maternal self-esteem at 24 months postpartum. Among these 349 pairs, 192 pairs were re-interviewed to assess children's adaptive ability and children's concurrent blood lead levels when the children were 7–15 years old, and the main reason for lost to follow-up was lack of time or the inconvenience of re-visiting to the clinic.

We obtained ethics approval from the Institutional Review Boards of the Harvard School of Public Health, Mount Sinai School of Medicine and attending hospitals, National Institute of Public Health of Mexico, University of Michigan, and University of Toronto. Women and children old enough signed informed consent letters at the initiation of study procedures.

### 2.2. The assessment of maternal self-esteem

When children were 24 months old, maternal self-esteem was measured using the Spanish version of the Coopersmith Self-Esteem Inventory (Adult Short Form). The inventory is a 25-item scale with good reliability and validity that measures an adult's overall subjective emotional evaluation toward his or her own worth in personal, social, family, and academic areas of experience (Surkan et al., 2008; Xu et al., 2015), and its internal consistency reliabilities (Cronbach-α around 0.77) and the test-retest reliabilities (around 0.80 over periods of 6–58 weeks) were acceptable (Gibbs and Norwich, 1985). Each item of the scale requires an answer of “like me” or “unlike me.” The total scores ranged from 1 to 25, and higher total scores indicate higher self-esteem levels.

### 2.3. Prenatal and current lead exposure measurements

Maternal bone lead concentrations were measured at the tibial midshaft and at the patella using a Cd-109 K-shell X-ray fluorescence

instrument (ABIOMED, Danvers, MA, USA). We used reference materials of plaster-of-Paris phantoms as targets for inter-calibration standards (Aro et al., 1994; Nie et al., 2004). Previous studies had validated K-shell X-ray fluorescence bone lead measurements by inductively coupled plasma mass spectrometry (Aro et al., 2000; Bellis et al., 2012; Weisskopf et al., 2010). Before the 30-min measurements, the bone sites were cleaned with a 50% solution of isopropyl alcohol. Maternal tibia and patella bone lead concentrations are considered as biomarkers of cumulative fetal lead exposure (Hu et al., 1998; Zhang et al., 2012). The patella lead and tibia lead have half-lives of several years and decades, respectively, and the patella lead has a higher bone-blood turnover rate than the tibia lead during pregnancy (Pilsner et al., 2009; Zhang et al., 2012).

Cord blood and children's current blood were collected in trace metal-free tubes based on standard operating manuals, and then shipped to the University of Michigan and stored at −80 °C until analyses. The cord blood lead was tested using an atomic absorption spectrometry (AAS, model 3000, PerkinElmer, USA) with a detection limit within 1 μg/dL, and children's concurrent blood lead was tested using inductively coupled plasma mass spectrometry (ICP-MS, Elan 6100, PerkinElmer, USA) with a detection limit of 0.03 μg/dL (Afeiche et al., 2012; Huang et al., 2016). All the blood lead levels were above the limit of detection. The same standard quality controls and external blinded quality control samples were both used in AAS and ICP-MS measurements.

### 2.4. The outcomes: the assessment of adaptive ability in children

The Behavior Assessment System for Children-Second Edition (BASC-2) is one of the main measures used to assess the adaptive behavior of children and adolescents (Adgent et al., 2014; Dowdy et al., 2011; Melnyk et al., 2004; Papazoglou et al., 2013). Child adaptive ability can be assessed using both the parent rating scales (PRS) and the Self-Reports of Personality (SRP) of the BASC-2. Parents completed PRS forms [at two age levels—child (ages 6 to 11) and adolescent (ages 12 to 21)] in about 10–15 min, children completed self-reported forms—child (ages 6 to 11) and adolescent (ages 12 to 21) in about 30 min. We used the validated Spanish version in this study. The PRS for children and for adolescents had the same five domains including activities of daily living (P-ADL), adaptability (P-ADA), functional communication (P-FC), leadership (P-LEA), and social skills (P-SS), to describe parent ratings of children's adaptive skills. The SRP for children and for adolescents also had the same four domains including self-reliance (SR), interpersonal relations (IR), relations with parents (RP), and self-esteem (SE), to indicate the self-ratings of children's adaptive behavior. Of the different components of the BASC-2 PRS and SRP, the internal consistency reliabilities and the test-retest reliabilities are good. The internal consistency reliabilities range from 0.80s to 0.90s, and increase with the age of the child, similar across gender. The one-month test-retest reliabilities are typically in the middle 0.80s to the middle 0.90s, but SRP has slightly lower test-retest reliabilities than PRS. The interrater reliabilities for PRS are about 0.57–0.74 (Reynolds and Kamphaus, 2004). The raw scores of the individual domains were converted to age-adjusted T-scores with a mean of 50 and a standard deviation of 10. T-scores indicated the differences of raw scores from the norm-group means. Higher T-scores indicated that children had better adaptive skills (Adgent et al., 2014; Dowdy et al., 2011; Melnyk et al., 2004; Papazoglou et al., 2013). Reviews of videotaped evaluations were done for the quality control checks.

### 2.5. Covariates

The demographic information of mother-child pairs including family economic level, marital status, maternal age at enrollment, years of maternal and paternal education, and the child's sex and age, was collected by the questionnaire. Because of a potential association between children's concurrent lead exposure and adaptive behavior, children's current blood lead was used as a covariate in all the multivariable regression models to adjust for the potential confounding effects due to concurrent lead exposure, and to focus on the effects of prenatal lead exposure.

### 2.6. Statistical analyses

After examining the data distribution, descriptive statistics were used to describe the basic features of exposures and outcomes of interest. Using simple linear regression, we quantified the unadjusted relationship between maternal self-esteem and child adaptive T-scores. Analyses examined maternal self-esteem in relation to P-SS, P-LEA, P-ADL, P-ADA, P-FC, SR, SE, RP and IR T-scores. The adjusted associations between maternal self-esteem and adaptive T-scores were explored by multivariable linear regression models.

We used interaction terms for maternal self-esteem by prenatal lead exposure in the adjusted models, and separate models using different prenatal lead exposure variables (maternal tibia lead, patella lead or cord blood lead) were estimated to assess the modifying effects of prenatal lead exposure on the relationship between maternal self-esteem and adaptive behavior. Although cord blood lead, maternal tibia and patella lead were continuous variables, they were categorized into quartiles to examine the effect of maternal self-esteem within strata of prenatal lead exposure.

After significant interactions between maternal self-esteem and prenatal lead exposure were observed, the relationship between maternal self-esteem and child adaptive ability was evaluated separately within each quartile of prenatal lead exposure. We finally showed the relationship between maternal self-esteem and adaptive T-scores among the high prenatal lead exposure group (mother-child pairs with the highest 3 quartiles of prenatal lead exposure, P25—P100) *vs* among the low prenatal lead exposure group (pairs with the lowest quartile, P1—P25), because we found that the magnitude of the association between maternal self-esteem and adaptive T-scores varied depending on the levels of prenatal lead exposure. Positive associations between maternal self-esteem and adaptive T-scores were observed when cord blood lead or maternal patella lead was in the lowest quartile, but no significant associations when cord blood lead or maternal patella lead fell in each of the 3 highest quartiles, therefore, the 3 highest quartiles were combined and defined as the high prenatal lead exposure group. Statistically significant interaction effect was identified if $P_{interaction} < 0.10$.

All the statistical analyses were conducted using SAS (version 9.2, SAS Institute Inc., Cary, NC, USA). We also plotted smoothed curves to visually present the relationship between maternal self-esteem and child adaptive behavior in the context of different levels of prenatal lead exposure via Spline smoothing plots using Empower(R) (version 2.13.9, X&Y solutions, Inc., Boston, MA) and R (version 2.15.3, Robert Gentleman and Ross Ihaka, Auckland, New Zealand).

## 3. Results

The demographic characteristics of the 192 mother-child pairs were shown in Table 1. No significant differences were observed in family socio-economic status, marital status, maternal self-esteem scores, gestational week, maternal bone lead, child sex and birth weight between mother-child pairs who were followed and those who were lost to follow-up. All the study women were Mexicans. On average, the mothers completed 10.3 years of schooling, their average age was 25.9 years old when being recruited, and 32.3% of the mothers were single. The ratio of boys to girls in our study children was 56.8% to 43.2%, and children's average age was 11.1 years old. The medians of the cord blood lead and children's concurrent blood lead were 5.5 and 2.7 μg/dL, and the medians of the maternal patella and tibia lead were 12.6 and 10.2 μg/g (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2495770/

**Table 1**
Basic Characteristics of the study mother-child pairs.

| Variables | N | Mean (SD) or Median (P25, P75) or N (%) |
|---|---|---|
| **Prenatal maternal factors** | | |
| Maternal age (yrs) | 192 | 25.9 (5.2) |
| Maternal education (yrs) | 190 | 10.3 (2.8) |
| Family economic level | 187 | 8.3 (3.7) |
| Marital status/Married: Single | 192 | 130 (67.7): 62 (32.3) |
| Maternal IQ | 186 | 90.1 (21.0) |
| Patella lead (μg/g) | 155 | 12.6 (3.2, 21.7) |
| Tibia lead (μg/g) | 128 | 10.2 (4.1, 16.0) |
| **Maternal self-esteem (when children were 2 yrs)** | 192 | 17.1 (4.8) |
| **Children's factors** | | |
| Boy: Girl | 192 | 109 (56.8): 83 (43.2) |
| Birth order | 192 | 2.3 (1.3) |
| Birth weight (g) | 192 | 3170.6 (435.0) |
| Age (yrs) | 192 | 11.1 (3.4) |
| Cord blood lead (μg/dL) | 119 | 5.5 (3.5, 8.1) |
| Current blood lead (μg/dL) | 148 | 2.7 (2.0, 4.0) |
| P-ADA | 192 | 49.6 (9.6) |
| P-SS | 192 | 45.6 (11.2) |
| P-LEA | 192 | 48.0 (10.6) |
| P-FC | 192 | 48.2 (9.7) |
| P- ADL | 192 | 47.4 (10.4) |
| SR | 118 | 50.4 (10.0) |
| IR | 118 | 53.1 (7.1) |
| RP | 118 | 49.9 (8.6) |
| SE | 118 | 51.3 (8.5) |

Abbreviations P-ADL, parent-reported activities of daily living; P-ADA, parent-reported adaptability; P-FC, parent-reported functional communication, P-LEA, parent-reported leadership; P-SS, parent-reported social skills; SR, self-reliance; IR, interpersonal relations; RP, relations with parents; SE, self-esteem.

table/T1/Table 1).

All the average PRS and SRP T-scores were within normal ranges (> 40). The T-scores of the five PRS adaptive domains were highly correlated with each other (Pearson correlation coefficients from 0.6 to 0.7, $P = .000$), and the T-scores of the four SRP domains had moderate correlations with each other (Pearson coefficients from 0.3 to 0.5, $P < 0.01$). However, except that SR had significant but low correlations with four of the five PRS domains (P-ADL, P-SS, P-FC, and P-LEA; Pearson coefficients from 0.2 to 0.3, $P < 0.05$), the correlations between T-scores of other SRP domains and all the five PRS T-scores kept non-significant (Pearson coefficients $\leq 0.1$, $P > 0.05$).

### 3.1. The association between maternal self-esteem and child adaptive ability

Table 2 showed the results of multivariable linear regression analyses. When adjusting for family economic status, marital status, maternal educational and age, child age and sex, and children's current blood lead levels, higher maternal self-esteem scores were significantly associated with higher P-LEA, P-ADL, P-FC, IR and RP T-scores ($P < 0.05$), and marginally associated with P-SS, P-ADA, and SR T-scores. 1-standard deviation increase in maternal self-esteem scores was associated with 2.9%–5.1% increase in adaptive T-scores. Only SE had no significant association with maternal self-esteem (Table 2).

### 3.2. Modifying effects of prenatal lead exposure on the relationship between maternal self-esteem and child adaptive ability

Spearman correlations between patella and tibia lead, patella and cord blood lead, and tibia and cord blood lead were 0.4 ($P = .000$), 0.4 ($P = .000$) and 0.2 ($P = .085$), respectively, and Spearman correlations between children's concurrent blood lead and any of prenatal lead exposure biomarkers were $\leq 0.1$ ($P > 0.05$). Whether in unadjusted or adjusted models, when stratified by cord blood lead, the positive relationships between maternal self-esteem scores and adaptive T-scores were more evident among the low prenatal lead exposure group (P1−P25) than among the high exposure group (P25−P100) ($P_{interaction}$ for P-SS, P-LEA, P-ADL, P-ADA, and SR were all < 0.10, results of adjusted models see Table 2 and Fig. 1). A similar pattern was observed for P-SS and P-LEA when stratified by patella lead ($P_{interaction}$ for P-SS and P-LEA were all < 0.10) (results of adjusted models see Table 2, Fig. 2). However, we didn't find significant interaction between self-esteem and cord blood lead/patella lead on P-FC, IR, RP and SE T-scores ($P > 0.10$, because small differences were observed in the association between the high and low cord blood lead/patella lead groups, graphs on IR, RP, and SE were not shown in Figs. 1 and 2). However, when stratified by tibia lead, no significant associations were found between maternal self-esteem and adaptive T-scores among both low and high tibia lead groups in unadjusted or adjusted models, and no significant interaction effects between self-esteem and tibia lead on any adaptive T-score were observed, suggesting cord blood lead or maternal patella lead (but not tibia lead) had potential modification roles in the relationship between maternal self-esteem when children were toddlers and adaptive abilities in school-aged children. To compare the impacts of missing values in cord blood lead/patella lead/tibia lead data on the unadjusted and adjusted results, we analyzed the demographic characteristics of the mother-child pairs with and without cord blood lead/patella lead/tibia lead data, and found that no significant differences were observed in maternal age, self-esteem scores, family socioeconomic status, marital status, child sex and current blood lead levels.

## 4. Discussion

As far as we know, this is the first prospective study evaluating maternal self-esteem as a predictor of children's future adaptive abilities, and also the first study evaluating the modifying effects of prenatal lead exposure on such an association.

This study found that maternal low self-esteem experienced during toddlerhood was associated with children's future adaptive skill deficits especially in the domains involving functional communication, daily living activities, leadership, relations with parents, and interpersonal relations, and probably in the domains involving social skills, adaptability and self-reliance. The deficits covered multiple dimensions relevant to personal independence (P-ADL, P-FC), adaptation to environments (P-ADA, P-SS, P-FC, IR) and social (P-LEA, P-SS, IR)/academic (SR)/family responsibility (RP). This finding was consistent with studies demonstrating that higher maternal distress levels experienced during childhood predicted lower self-efficacy in emerging adult offspring (Nilsen et al., 2016), and consistent with studies reporting that teen daughters of chronically distressed mothers were more likely be particularly reckless decision-makers (Flouri et al., 2017).

Mothers setting sub-optimal behavioral examples; mothers manifesting pathological defense mechanisms; children having reduced empathy to maternal distress, and genetics may be the major potential mechanisms underlying the association between maternal self-esteem and children's future adaptive abilities (Creswell et al., 2005; Porcerelli et al., 2016; Xu et al., 2015). First, mothers with lower self-esteem are usually less likely to actively seek social support. Mothers with lower self-esteem usually have lower ability to adaptively cope with stressors, and they therefore set a sub-optimal example for their children on how to react to conflicts and challenges in their future (Porcerelli et al., 2016). Second, the defense mechanism refers to the automatic psychological process that mediates responses to internal or external stressors (Porcerelli et al., 2016). Mothers with low self-esteem usually have pathological defense mechanisms and tend to ignore the thoughts and feelings of their children. This may promote children's excessive desire to maintain proximity with their mothers and force children to develop a less adaptive strategy, and this may be associated with greater social-emotional and behavioral regulatory problems in the children in later years (Creswell et al., 2005; Porcerelli et al., 2016).

**Table 2**
Adjusted[a] differences [β (SE)] in T-scores of children's adaptive scales for one-point increase in maternal self-esteem scores.

| Adaptive scales | Overall effects: $\beta_{self\text{-}esteem}$ (N = 143) | Effect modification[b] by cord lead: $\beta_{self\text{-}esteem}$ (N = 102) | | | Effect modification[b] by patella lead:$\beta_{self\text{-}esteem}$ (N = 119) | | |
|---|---|---|---|---|---|---|---|
| | | Low[c] cord-lead (≤3.5 μg/dL) | High[c] cord-lead (> 3.5 μg/dL) | $P_{interact}$[d] | Low[c] patella lead (≤3.2 μg/g) | High[c] patella lead (> 3.2 μg/g) | $P_{interact}$[d] |
| P-SS | 0.4 (0.2) | 1.4 (0.3)*** | 0.1 (0.3) | 0.004† | 1.1 (0.4)* | 0.2 (0.2) | 0.07† |
| P-LEA | 0.4 (0.2)* | 1.2 (0.3)*** | 0.2 (0.2) | 0.02† | 1.0 (0.4)* | 0.2 (0.2) | 0.07† |
| P-ADL | 0.5 (0.2)* | 1.3 (0.4)*** | 0.1 (0.3) | 0.007† | 1.0 (0.4)* | 0.3 (0.3) | 0.18 |
| P-ADA | 0.4 (0.2) | 1.1 (0.3)*** | 0.2 (0.2) | 0.03† | 0.5 (0.4) | 0.3 (0.2) | 0.55 |
| P-FC | 0.4 (0.2)* | 0.9 (0.3)** | 0.5 (0.2)* | 0.26 | 0.9 (0.4)* | 0.2 (0.2) | 0.15 |
| SR[e] | 0.4 (0.2) | 0.9 (0.4)* | 0.0 (0.3) | 0.08† | 0.4 (0.4) | 0.2 (0.3) | 0.66 |
| IR[e] | 0.3 (0.1)* | 0.3 (0.2) | 0.3 (0.2) | 0.89 | 0.3 (0.3) | 0.2 (0.2) | 0.73 |
| RP[e] | 0.4 (0.2)* | 0.5 (0.3) | 0.4 (0.2) | 0.81 | 0.4 (0.4) | 0.4 (0.2) | 0.95 |
| SE[e] | 0.2 (0.2) | 0.2 (0.3) | 0.2 (0.2) | 0.95 | 0.1 (0.3) | 0.2 (0.2) | 0.86 |

*Abbreviations:* P-ADL, parent-reported activities of daily living; P-ADA, parent-reported adaptability; P-FC, parent-reported functional communication, P-LEA, parent-reported leadership; P-SS, parent-reported social skills; SR, self-reliance; IR, interpersonal relations; RP, relations with parents; SE, self-esteem.

[a] Models were controlled for family economic status, marital status, maternal education and age, child's sex and age, and children's current blood lead. †$P < 0.1$; *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

[b] In addition to adjustment factors, models for effect modification included cord blood (or patella) lead category (high/low), self-esteem, and the interaction between cord blood (or patella) lead and self-esteem.

[c] Lead categories were defined based on the 25th percentile (P25) of the lead distribution (i.e., P25 = 3.5 μg/dL for cord lead and P25 = 3.2 μg/g for patella lead).

[d] $P_{interact}$ was the *P*-values for the interaction terms and indicated the difference in self-esteem coefficients comparing low *vs* high prenatal lead exposure group.

[e] N = 108 for overall models, N = 95 for models assessing effect modification by cord lead, N = 97 for models assessing effect modification by patella lead.

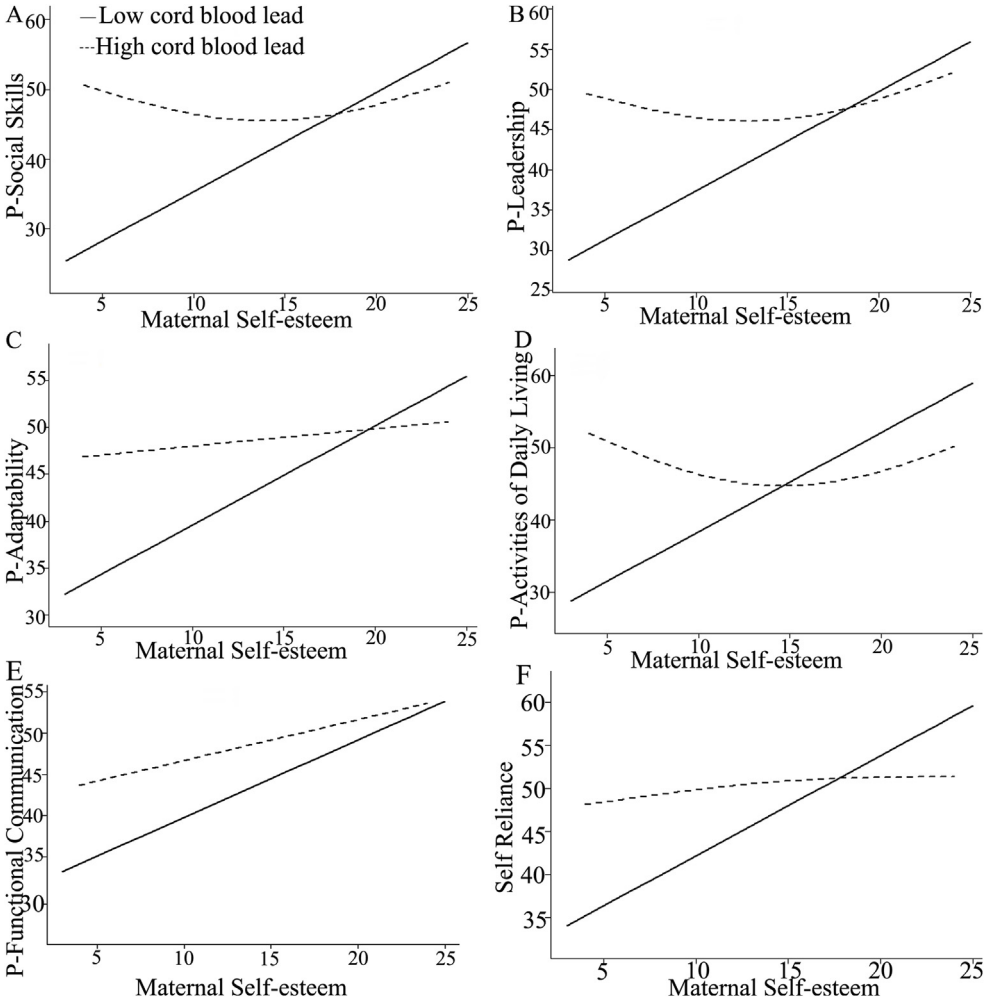


**Fig. 1.** Adjusted relationships between maternal self-esteem and adaptive T-scores when stratified by cord blood lead. The comparison between the lowest quartile of cord blood lead (P1—P25, full line) and the highest 3 quartiles (P25—P100, dotted line) was shown. $P_{interaction}$ values < 0.10 for all the subscales except for P-Functional Communication.

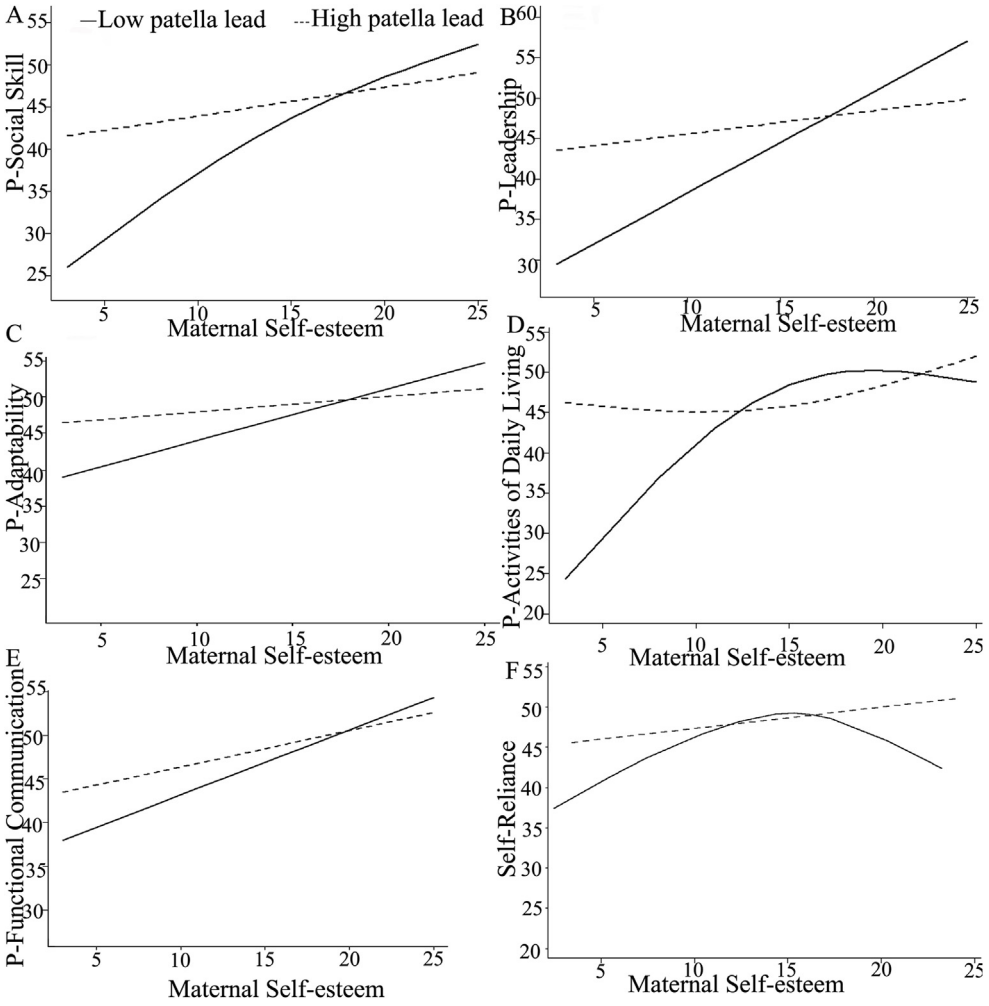


**Fig. 2.** Adjusted associations between maternal self-esteem and adaptive T-scores when stratified by maternal patella lead. The comparison between the lowest quartile of patella lead (P1—P25, full line) with the highest 3 quartiles (P25—P100, dotted line) was shown. $P_{interaction}$ values for P-social skills and P-Leadership were < 0.10.

Third, children having mothers with low self-esteem usually suffer a negative mother-child relationship (Porcerelli et al., 2016). This negative relationship fosters negative socialization trajectories, and may in turn cause children's weak empathy to maternal distress and be associated with adaptive problems in their future (Kochanska et al., 2010). Fourth, mothers with low self-esteem developing emotional or social maladjustment may have related gene deficits. Accordingly, genetics may play a role in the development of children's negative adaptive behavior (Pierpont et al., 2010).

Compared with using SRP adaptive T-scores as the outcomes, we found stronger associations between maternal self-esteem and adaptive abilities and stronger interaction between maternal self-esteem and cord blood lead/patella lead if PRS adaptive T-scores were used as the outcomes, which may be related to differences in report bias (children's self-reported rates of difficulties were usually lower than parent-reported rates, and children tended to underreport their symptomatology (Perfect et al., 2013)), psychometric properties (PRS had slightly higher reliabilities than SRP) and statistic power (because SRP data were less than PRS data in this study, the models using SRP T-scores as the outcomes would have less statistic power than the models using PRS T-scores as the outcomes).

Our study also demonstrates that prenatal lead exposure attenuates the positive effects of maternal high self-esteem on child adaptive ability, which means that a child's possibly high adaptive ability associated with high maternal self-esteem could be nipped in the bud if the mother experiences a high level of prenatal lead exposure. Consistent with the present results, previous findings from this same longitudinal birth-cohort study have shown that prenatal lead exposure modifies the association of maternal self-esteem with toddlers' cognitive abilities (Surkan et al., 2008), and the association of maternal self-esteem with children's future inattention behavior (Xu et al., 2015). In contrast to cord blood lead, which possesses a mean biological life of around one month, and reflects levels of fetal recent exposure to lead or the recent mobilization of lead from maternal skeleton into the circulation without ongoing external lead exposure (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295346/Hu et al., 1998), maternal tibia and patella bone lead concentrations represent maternal cumulative lead exposure levels (Hu et al., 1998; Zhang et al., 2012). The patella lead is superior to tibia lead in its correlation with maternal and cord blood lead levels, and generally considered to correlate more closely with levels of embryo/fetal exposure to lead than the tibia lead during the entire pregnancy (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295346/Hu et al., 1998; Pilsner et al., 2009; Zhang et al., 2012). The observed modifying effects of cord blood lead and patella lead make us to speculate that the modifying effects are directly related to prenatal lead exposure stemming from maternal trabecular bone (the compartment of bone from which lead is most mobilizable) (Hu et al., 1998), and the lead impacts on child brain programming may begin early in embryonic or fetal development stage.

Previous animal studies reported that potential mechanisms

underlying the interaction may involve the targeting by lead and stress of common systems in the central nervous system. Both lead and stress induce neurochemical changes in some of the brain regions and neurotransmitter systems mediating offspring behavioral flexibility or emotion control (Cory-Slechta et al., 2013b; Kordas et al., 2011; Weston et al., 2014), such as decreased serotonin function in mesocorticolimbic regions, monoamine changes in nucleus accumbens, and increased expression in serotonin transporters in the front cortex. In addition, as the key targets of lead effects on child behavior, some brain systems closely associated with child behavioral/emotional control or responses to stress such as the mesocorticolimbic serotonin system have extensive interactions with the hypothalamic-pituitary-adrenal axis (Cory-Slechta et al., 2008).

The strengths of this study include a long-running longitudinal study design and comprehensive evaluations of socioeconomic status and prenatal lead exposure. Three indexes including cord blood lead, maternal tibia lead and patella lead levels were applied in this study to fully account for levels of prenatal lead exposure (Xu et al., 2015). Children's adaptive ability was assessed by all the five BASC-2 PRS Adaptive Skill subscales, and 61.5% of children in this study were additionally assessed by the BASC-2 SRP Adaptive Skill subscales. Our confidence in the findings is strengthened by the consistency in the effects between any two of the five PRS Adaptive Skill subscales and between PRS and SRP Adaptive Skill subscales. Another advantage of this study is that, children's concurrent blood lead levels were adjusted to specially focus on the impact of prenatal lead exposure. In addition, based on statistical and biological considerations, a variety of confounders were controlled in this study, however, the adjustment didn't significantly change the magnitudes of most estimates, indicating that the effects observed in this study were relatively stable.

Our study also had some limitations. First, we have relatively small sample size, which make our statistical power limited. Second, our study was performed among a Mexican population with a low to moderate socioeconomic level, and we cannot generalize our findings to the population at the highest ends of the socioeconomic spectrum. Further studies conducted in other populations are warranted. Third, biomarkers of stress have been used to assess the stress levels. However, because of variability of levels of stress biomarkers due to diurnal rhythm (Serón-Ferré et al., 2001), the adrenal stress index curve test can comprehensively reflect stress levels. Therefore, it may be best to evaluate human stress using both well-validated scales and the adrenal stress index curve test (Serón-Ferré et al., 2001). In this study, maternal self-esteem was evaluated using the validated scale, but the adrenal stress index curve test was not done. Fourth, bias may have been introduced due to the loss of follow-up of participating subjects or missing values in the follow-up data. Fifth, although the fact that mothers were blinded to their self-esteem scores and lead results made the BASC-2 parental ratings on the children's adaptive skills more reliable, we didn't collect information on teacher ratings of children's adaptive skills, and the teacher ratings may be less subjective than the parental ratings (Dowdy et al., 2011; Papazoglou et al., 2013). Sixth, we didn't measure concurrent maternal self-esteem levels, however, because self-esteem is a stable, trait-like construct (Trzesniewski et al., 2003), confounding due to not adjusting for maternal concurrent self-esteem levels may be partially controlled by the inclusion of maternal self-esteem levels when children were 2 years old (the main predictor) in our regression models. Seventh, inconsistent findings were reported on the role of pubertal development in the association between maternal stress and children's adaptive abilities. One previous study showed that the association between maternal chronically high psychological distress and girls' decision-making pathology was similar for girls who had reached puberty and those who had not (Flouri et al., 2017). However, other studies reported that negative child-mother relationships associated with maternal distress may predict earlier timing of pubertal development (Belsky et al., 2007; Costello et al., 2007; Ellis, 2004; Thelus Jean et al., 2009), which might be associated with more emotional problems or high-risk behaviors in children (Costello et al., 2007). In this study, we didn't compare the association between maternal self-esteem and children's future adaptive abilities among children/adolescents before and during puberty. Finally, we only assessed the main effects of maternal self-esteem and the modifying effects of prenatal lead exposure but have no information on genetic markers linked to the adaptive skill. Therefore, our study provides suggestive but inconclusive evidence for the effects.

## 5. Conclusions

Our study suggests that toddlers of mothers with higher self-esteem levels may be more likely to develop higher adaptive skills at school age. However, prenatal lead exposure may interfere against this positive effect. Our findings emphasize the importance to prevent pregnant women from lead exposure. Because children will inevitably face multiple challenges after their transition from the family to extended social ecologies, children with better adaptive skills will have a greater developmental advantage. Therefore, studies those focusing on children's adaptive skills that may promote such a trajectory continue to be significant. Longitudinal studies with larger sample sizes are warranted to confirm the associations and the potential effect-modification observed in this study.

## Competing financial interests

The authors declare no competing interests.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijheh.2018.08.005.

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