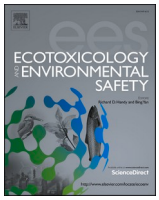
Ecotoxicology and Environmental Safety 311 (2026) 119845

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv



Early childhood blood lead concentrations and selective attention among school-age children: Evidence consistent with a causal association and effect modification by sleep duration

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ARTICLE INFO

Edited by Dr. Renjie Chen

Keywords:
Blood lead
Stroop Color and Word Test
Children
Generalized propensity score
Doubly robust estimation
Cohort

ABSTRACT

Selective attention is essential for cognitive and behavioral self-regulation. However, the association between lead exposure and selective attention remains unclear. We examined the association between blood lead levels and selective attention, and evaluated whether this association is influenced by sleep duration. We used data from a prospective cohort of 377 Korean children. Blood lead concentrations and Stroop Color and Word Test (SCWT) scores were repeatedly measured at 6, 8, and 10 years of age. Generalized propensity scores (GPSs) were generated using linear regression models predicting lead levels. Associations between lead levels and SCWT scores were assessed using causal inference approaches, such as linear mixed models adjusted for both GPS and potential confounders, as well as doubly robust estimation models. In models adjusted for both GPS and potential confounders, a doubling of lead levels was associated with lower color [β = -1.46, 95 % confidence interval (CI): −2.63, −0.30] and color–word (β = −1.52, 95 % CI: −3.00, −0.04) test scores. In doubly robust models, these associations persisted for the color (β = −1.35, 95 % CI: −2.36, −0.34) and color–word (β = −1.33, 95 % CI: −2.61, −0.04) test scores. The associations varied by sleep duration, with stronger effects observed among children sleeping ≤ 8 h compared with those sleeping longer. By applying multiple causal inference approaches, this study provides robust evidence that lead exposure impairs selective attention in school-age children. The detrimental associations were amplified among those sleeping ≤ 8 h, suggesting that sufficient sleep may mitigate the neurotoxic effects of lead exposure.

1. Introduction

Selective attention—the ability to concentrate on goal-relevant stimuli while suppressing distraction—is essential for cognitive and behavioral self-regulation (Fisher, 2019). Impaired selective attention in early life is associated with increased risk of academic underperformance, classroom behavioral issues, and reduced social competence, and may contribute to long-term outcomes such as lower

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https://doi.org/10.1016/j.ecoenv.2026.119845
Received 3 September 2025; Received in revised form 4 February 2026; Accepted 4 February 2026
Available online 6 February 2026

educational attainment, mental health difficulties, and impaired occupational functioning (Rabiner et al., 2016; Stevens and Bavelier, 2012). Because current interventions primarily manage symptoms rather than restore attentional capacity, identifying and mitigating early-life risk factors for impaired selective attention is a critical public health priority.

Environmental exposure to lead, an established neurotoxicant, has been associated with a variety of neurodevelopmental outcomes, including deficits in cognitive function and behavioral problems, even at blood lead concentrations below 5 μg/dL. However, the association between lead exposure and selective attention remains uncertain, with inconsistent findings across studies; some reported significant associations (Kim et al., 2010; Schwartz et al., 2000), whereas others found no association (Choi et al., 2020; Surkan et al., 2007; Yu et al., 2019, 2021). Furthermore, to the best of our knowledge, no prior study has applied causal inference methodologies (e.g., propensity score methods and doubly robust estimation) to rigorously evaluate the causal relationship between low-level lead exposure and neurodevelopmental outcomes, raising concerns of residual confounding inherent to observational study designs.

Inadequate sleep duration, particularly shorter sleep, has been linked to reduced selective attention in both younger and older adults (Asaoka et al., 2025; Song et al., 2023; Wiggins et al., 2018), although evidence among school-age children remains limited. Given this adverse impact of insufficient sleep on selective attention, sleep duration may modify the association between lead exposure and selective attention, with stronger effects expected among children with shorter sleep duration. However, to the best of our knowledge, this potential effect modification has not been investigated, despite its important implications for developing public health strategies to reduce the neurotoxic burden of lead.

Therefore, we investigated the association between blood lead levels and selective attention and evaluated whether this association is modified by sleep duration using a prospective birth cohort of Korean children followed up to age 10 years. To strengthen causal interpretation, we applied causal inference approaches to observational data. We hypothesized that blood lead levels would be causally associated with lower selective attention in school-age children, and that this association would be stronger among those with inadequate sleep duration compared with those with adequate duration.

2. Materials and methods

2.1. Data source and study participants

The present study used data from the Environment and Development of Children (EDC) study, an ongoing cohort designed to investigate associations between prenatal and postnatal environmental exposures and children's physical and neurobehavioral health outcomes. Detailed information on the study design and protocol has been described elsewhere (Kim et al., 2018). Briefly, 703 pregnant women without genetic or immunodeficiency disorders and with sufficient Korean language proficiency were recruited during the second trimester from eight hospitals in Seoul and Gyeonggi province, Republic of Korea (August 2008–July 2010). The children of the enrolled mothers have been followed biennially since 2012 at ages 2, 4, 6, 8, and 10 years. Concentrations of pollutants were measured using maternal blood and urine samples during pregnancy and child samples at each follow-up. Various physical and neurobehavioral outcomes were also assessed, with selective attention evaluated using the Stroop Color and Word Test (SCWT) administered by trained clinical psychologists at 6, 8, and 10 years of age.

Of the 572 children assessed at 6 years of age, we excluded 79 with missing prenatal blood lead data, 56 with missing blood lead data at both 2 and 4 years, and 3 with missing blood lead data at all three time points of 6, 8, and 10 years. We further excluded 44 children with missing SCWT data at all three time points of 6, 8, and 10 years, 11 children with missing covariate data (maternal smoking during pregnancy), and 2 with missing data for a variable (birth order) used to estimate generalized propensity scores (GPSs). The final analytical sample consisted of 377 children at 6 years, of whom 348 were followed up at 8 years and 306 at 10 years.

The Institutional Review Board of Seoul National University Hospital approved the study protocol (IRB No. 1201–010–392). The study adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from parents of all participants and additionally from children at ages 8 and 10 years.

2.2. Measurement of blood lead concentrations

Whole blood samples were collected from mothers during pregnancy (14–27 weeks of gestation) and from children at 2, 4, 6, 8, and 10 years of age in ethylenediaminetetraacetic acid (EDTA) tubes. After collection, samples were stored at −20 ℃ until analysis. Prior to measurement, samples were thawed to room temperature and homogenized using a vortex mixer. Blood samples were then diluted with a matrix modifier containing 20 % ammonium phosphate monobasic ($NH_4H_2PO_4$) and Triton X-100 (Sigma-Aldrich, MO, USA). Quantification of lead was performed using a Zeeman atomic absorption spectrometer (240Z AA, Agilent Technologies, CA, USA), applying the standard addition method with Environmental Calibration Standards (Part #5183–4688, Agilent) to control for matrix effects.

The limits of detection (LODs) ranged from 0.092 to 0.282 μg/dL across sampling waves, and all blood samples had lead concentrations above the LOD.

2.3. Evaluation of selective attention

Selective attention was assessed at ages 6, 8, and 10 years using the SCWT, a widely employed neuropsychological instrument and a well-validated measure of selective attention. Originally developed by Charles Gordon for children aged 5–14 years (Shin and Park, 2007), the SCWT has been frequently applied to evaluate selective attention in both the general population and in various neurodevelopmental conditions, including attention-deficit/hyperactivity disorder, autism spectrum disorder, specific learning disorders, and tic disorders. The SCWT consists of three 45-second trials: a word-reading condition (reading color names printed in black ink), a color-naming condition (naming the ink color of presented color patches or symbols), and an incongruent color–word condition (naming the ink color of a color word that spells a different color). Successful performance requires attending to the task-relevant attribute (e.g., ink color) while ignoring conflicting or irrelevant information (e.g., word meaning).

In this study, the Korean standardized children's version of the SCWT (Shin and Park, 2007) was administered by trained clinical psychologists from Seoul National University Hospital. Children were instructed to respond aloud as quickly and accurately as possible. Three performance indices were obtained based on the accuracy of each trial (word, color, and color–word test scores). Raw scores were then converted into age- and sex-adjusted T-scores (mean = 50, standard deviation = 10), with higher scores indicating better selective attention.

2.4. Assessment of sleep duration

Children's average sleep duration was assessed in surveys at ages 6, 8, and 10 years. Parents were asked to report the child's usual total sleep duration over a typical week, reflecting an average of weekday and weekend sleep. To capture potential non-linear effects and ensure sufficient sample sizes within each category, sleep duration was classified into three groups: ≤ 8 h, > 8 to < 10 h, and ≥ 10 h. This categorical variable was incorporated in the analyses as a time-varying variable. There were no missing data.

2.5. Covariates and predictors of generalized propensity scores

Based on previous epidemiological studies (Choi et al., 2020; Kim et al., 2010; Schwartz et al., 2000; Surkan et al., 2007; Takeuchi et al., 2021; Yu et al., 2019, 2021), the following potential confounders were identified and adjusted for in analytical models: child's age (month) and sex, maternal age at enrollment (year), maternal educational level (≤high school graduate, college or university, or graduate school), maternal smoking during pregnancy (never, past, or current smoker), and child's secondhand smoke exposure (no or yes). Information on these variables were collected at each child survey (child's age, sex, and secondhand smoke exposure) or at maternal enrollment (maternal age, educational level, and smoking during pregnancy). Child's age and secondhand smoke exposure were modeled as time-varying covariates.

GPS methods extend conventional propensity score approaches to continuous exposures by balancing measured covariates across exposure levels. To generate GPSs, the above confounders were included together with additional predictors of lead exposure identified in prior studies (Carrel et al., 2017; Taylor et al., 2013): housing type (single-family, multi-family, apartment, or other), distance from major roads (≥500 m, 100–499 m, 50–99 m, or <50 m), presence of nearby factories (no or yes), presence of a nearby waste incineration plant (no or yes), and birth order (ordinal). Information on these variables was collected at child surveys (ages 2, 4, 6, 8, and 10 years) and treated as time-varying variables.

No missing data were observed for either the potential confounders or the predictors of lead exposure.

2.6. Statistical analysis

Because blood lead concentrations exhibited a right-skewed (approximately log-normal) distribution, they were summarized using geometric means and geometric standard deviations and $\log_2$-transformed for subsequent analyses.

To evaluate the associations between lead levels and repeatedly measured SCWT scores at ages 6, 8, and 10 years, we constructed linear mixed models with a random intercept for each participant. The models were adjusted for potential confounders and simultaneously included lead levels during pregnancy, the average of lead levels at ages 2 and 4 years, and repeatedly measured lead levels at 6, 8, and 10 years. By mutually adjusting for exposures at different time points, we aimed to disentangle independent effects and identify sensitive exposure windows.

To generate GPS, we first constructed a linear model predicting log-transformed lead levels using independent variables described above. We then estimated the GPS of each participant as:

GPS_i = MultiNormal(Y_i, mean = fitted values, standard deviation (SD) = SD of residuals),

where Y_i represents log-transformed lead levels of individual i at ages 2, 4, 6, 8, and 10 years. Fitted values and SD of residuals were derived from the prediction model.

Stabilized inverse probability weights (IPWs) were then calculated as:

$$IPW_i = \frac{Nulli}{GPSi},$$

where $Null_i$ = MultiNormal(Yi, mean = overall mean of pollutants, SD = overall SD). To reduce the influence of extreme weights, IPW values above the 99th percentile were truncated as the 99th, and those below the 1st percentile were truncated as the 1st.

To evaluate the positivity assumption for the GPS—requiring that every observation has a non-zero probability of receiving any given exposure level—we compared GPS distributions between participants with blood lead levels above and equal to the median and those below (Giffin et al., 2023). We found that the GPS distribution in both groups exhibited substantial overlap, supporting the assumption (Fig. S1). We also assumed that the consistency assumption—meaning that an individual's SCWT outcome is unaffected by other participants' lead exposure—and the absence of unmeasured confounding were reasonably satisfied (Giffin et al., 2023), as it is unlikely that one child's lead exposure would influence another child's Stroop test outcome, and we adjusted for a wide range of potential confounders.

To estimate causal effects, we applied three modeling strategies: (1) linear mixed models adjusted for GPS (continuous) only, (2) linear mixed models adjusted for both GPS (continuous) and confounders, and (3) doubly robust models adjusted for confounders and weighted by stabilized IPWs. Because GPS balances measured covariates across different levels of a continuous exposure, GPS adjustment helps approximate a counterfactual framework (Austin, 2018). Doubly robust estimation combines GPS weighting and outcome regression, yielding consistent effect estimates as long as either the exposure model or the outcome model is correctly specified (Bang and Robins, 2005).

To further probe potential bias from unmeasured confounding, we performed a negative control outcome analysis. This approach relies on an outcome not causally affected by exposure but is expected to share a similar confounding structure with both the exposure and the primary outcome. Given that lead exposure is not biologically expected to affect physical activity levels, and that physical activity is influenced by common potential confounders such as socioeconomic status, housing environment, and educational level (Pouliou et al., 2015; Tandon et al., 2012; Ziegeldorf et al., 2024), we selected the duration of moderate-intensity physical activity (activities causing a noticeable increase in heart rate and breathing while conversation; e.g., brisk walking, active play) as the negative control outcome.

We also examined associations between lead concentrations during pregnancy and at ages 2 and 4 years and SCWT scores at ages 6, 8, and 10 years using linear mixed models adjusted for both GPS and potential confounders, as well as doubly robust models, without adjustment for exposures at later ages (6, 8, and 10 years).

Stratified analyses were conducted by sex and sleep duration (≤8 h, >8 to <10 h, and ≥10 h) to explore potential differences in the associations between lead concentrations and SCWT scores.

In additional exploratory analyses, we examined the associations of blood lead levels with sleep duration (continuous) and of sleep duration (both continuous and categorical) with SCWT scores, using linear mixed models with the same adjustment structure.

We performed a sensitivity analysis that excluded adjustment for age and sex and did not include these variables in the GPS model, since the SCWT T-scores were already standardized for age and sex.

Because this study was based on an established birth cohort, no a priori power calculation was performed. To aid interpretation of the interaction analyses, we conducted simulation-based power calculations using the fitted mixed-effects models, preserving the observed sample size, repeated-measures structure, and covariate distribution. The within-child correction (ICC) was estimated from the random-intercept model, and power was evaluated across a range of standardized interaction effect sizes.

Data management, statistical analyses, and figure generation were conducted in R (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria) using the *dplyr*, *tidyr*, *lme4*, *lmerTest*, *dlnm*, *psych*, and *ggplot2* packages.

3. Results

Among the 377 children assessed at age 6 years, 192 (50.9 %) were boys. The mean maternal age at enrollment was 31.4 years. Mothers of 277 children (73.5 %) had attained a college or university education, and 20 mothers (5.3 %) reported smoking during pregnancy. A total of 82 children (21.8 %) were reported to have been exposed to secondhand smoke. Children sleeping > 8 to < 10 h were more likely to have mothers with at least a college education (88.1 %) compared with those

sleeping ≤ 8 h (74.3 %) (Table 1).

Geometric means ± geometric SDs of lead concentrations were 1.3 ± 1.3 μg/dL during pregnancy, 1.6 ± 1.4 μg/dL at age 2 years, 1.4 ± 1.4 μg/dL at age 4 years, 1.5 ± 1.4 μg/dL at age 6 years, 1.0 ± 1.5 μg/dL at age 8 years, and 1.0 ± 1.4 μg/dL at age 10 years (Table S1).

Blood lead concentrations during pregnancy were not correlated with postnatal levels (all *p*-values ≥0.05). In contrast, concentrations measured at 2, 4, 6, 8, and 10 years of age showed low to moderate positive correlations, with Pearson's correlation coefficients ranging from 0.23 to 0.47. Exceptions were observed for correlations between 2 and 8 years and between 2 and 10 years (both *p*-values ≥0.05) (Table S2). The intraclass correlation coefficient (ICC) for blood lead concentrations from ages 2–10 years was 0.23 [95 % confidence interval (CI): 0.19, 0.27], indicating low within-child reproducibility over time.

A doubling of lead levels at ages 6, 8, and 10 years was associated with lower SCWT scores at the same ages across multiple modeling approaches. In conventional linear mixed models adjusted for potential confounders, higher lead levels were linked to lower color test scores (β = −1.45, 95 % CI: −2.62, −0.28). In models adjusted for only GPS, higher lead levels were associated with lower word (β = −3.61, 95 % CI: −4.71, −2.52), color (β = −2.63, 95 % CI: −3.64, −1.61), and color–word (β = −3.03, 95 % CI: −4.34, −1.72) test scores. In models adjusted for both GPS and confounders, higher lead levels were associated with lower color (β = −1.46, 95 % CI: −2.63, −0.30) and color–word (β = −1.52, 95 % CI: −3.00, −0.04) test scores. In doubly robust models, these associations persisted for the color (β = −1.35, 95 % CI: −2.36, −0.34) and color–word (β = −1.33, 95 % CI: −2.61, −0.04) test scores (Table 2). No associations were observed between blood lead levels and the duration of moderate-intensity physical activity, which was used as the negative control outcome (Table S3).

Analyses of lead concentrations during pregnancy and at ages 2 and 4 years as exposures, without adjustment for later exposures (6, 8, and 10 years), showed that blood lead levels at age 2 years were associated with lower color test scores, whereas levels at age 4 years were associated with lower word, color, and color–word test scores. These associations were consistently observed in both the GPS- and confounder-adjusted models and in the doubly robust models. In addition, in the doubly robust model, lead levels at age 2 years were also associated with lower word test scores (Table S4).

In sex-stratified analyses, the associations between lead levels at ages 6, 8, and 10 years and SCWT scores at the same ages—particularly color–word test scores—were generally stronger among girls than boys. However, these findings should be interpreted with caution given the overlapping CIs (Table S5).

The associations between blood lead levels and SCWT scores differed

Table 1
Characteristics of study participants at age 6 years[a].

Characteristics	Total (*n* = 377)	Sleep duration		
		≤ 8 h (*n* = 35)	8–10 h[b] (*n* = 160)	≥ 10 h (*n* = 182)
Child's age (month)	71.1 ± 1.7	71.4 ± 1.8	71.2 ± 1.6	70.9 ± 1.7
Child's sex				
Boys	192 (50.9)	18 (51.4)	78 (48.8)	96 (52.7)
Girls	185 (49.1)	17 (48.6)	82 (51.3)	86 (47.3)
Maternal age at enrollment (year)	31.4 ± 3.4	31.7 ± 3.9	31.9 ± 3.5	30.8 ± 3.2
Maternal educational level				
≤High school graduate	51 (13.5)	9 (25.7)	19 (11.9)	23 (12.6)
College or university	277 (73.5)	22 (62.9)	116 (72.5)	139 (76.4)
Graduate school	49 (13.0)	4 (11.4)	25 (15.6)	20 (11.0)
Maternal smoking during pregnancy				
Never smoker	218 (57.8)	21 (60.0)	81 (50.6)	116 (63.7)
Past smoker	139 (36.9)	11 (31.4)	72 (45.0)	56 (30.8)
Current smoker	20 (5.3)	3 (8.6)	7 (4.4)	10 (5.5)
Child's secondhand smoke exposure				
No	295 (78.2)	28 (80.0)	121 (75.6)	146 (80.2)
Yes	82 (21.8)	7 (20.0)	39 (24.4)	36 (19.8)
Blood lead concentrations (μg/dL)	1.5 ± 1.4	1.5 ± 1.4	1.5 ± 1.4	1.4 ± 1.3
Stroop color and word test				
Word score	43.3 ± 11.6	41.0 ± 12.2	43.5 ± 10.9	43.5 ± 12.0
Color score	49.4 ± 10.7	49.0 ± 12.2	49.1 ± 10.5	49.7 ± 10.7
Color–word score	49.2 ± 13.4	48.4 ± 13.5	48.5 ± 12.0	50.0 ± 14.5

Continuous variables (excluding blood lead concentrations) are presented as mean ± standard deviation, while blood lead concentrations are presented as geometric mean ± geometric standard deviation, reflecting their right-skewed (log-normal) distribution. The geometric standard deviation represents a multiplicative dispersion rather than an absolute deviation and should not be interpreted as an arithmetic standard deviation. Categorical variables are shown as *n* (%).

[a] Participant characteristics are presented using data collected at age 6 years. The Stroop color and word test was administered repeatedly at ages 6, 8, and 10 years. The EDC birth cohort was recruited during the prenatal period and followed up at ages 2, 4, 6, 8, and 10 years.

[b] 8–10 h indicates sleep duration > 8 h to < 10 h.

Table 2
Associations between prenatal and postnatal blood lead concentrations and Stroop color and word test T-scores among children aged 6–10 years.

Blood lead levels	Word score		Color score		Color–word score	
	β	95 % CI	β	95 % CI	β	95 % CI
Adjusted for confounding factors[a]						
Prenatal	-0.85	-3.19, 1.50	-1.35	-3.72, 1.02	-0.81	-3.36, 1.73
2–4 years	-0.62	-2.81, 1.57	-1.08	-3.29, 1.13	-1.55	-3.93, 0.84
6–10 years	-0.56	-1.72, 0.61	-1.45	-2.62, -0.28	-1.41	-2.89, 0.08
Adjusted for generalized propensity score[b]						
Prenatal	-0.51	-2.74, 1.71	-1.16	-3.37, 1.06	-1.35	-3.76, 1.06
2–4 years	0.38	-1.78, 2.53	-0.94	-3.08, 1.21	-1.13	-3.47, 1.21
6–10 years	-3.61	-4.71, -2.52	-2.63	-3.64, -1.61	-3.03	-4.34, -1.72
Adjusted for generalized propensity score and confounding factors						
Prenatal	-0.82	-3.16, 1.52	-1.47	-3.79, 0.85	-0.97	-3.51, 1.57
2–4 years	-0.82	-3.00, 1.36	-1.44	-3.61, 0.73	-1.73	-4.11, 0.65
6–10 years	-0.58	-1.74, 0.59	-1.46	-2.63, -0.30	-1.52	-3.00, -0.04
Doubly robust estimation[c]						
Prenatal	-0.48	-2.83, 1.87	-1.34	-3.63, 0.95	-1.13	-3.69, 1.42
2–4 years	-1.17	-3.36, 1.01	-1.65	-3.78, 0.48	-2.25	-4.64, 0.14
6–10 years	-0.51	-1.53, 0.50	-1.35	-2.36, -0.34	-1.33	-2.61, -0.04

Associations were estimated using linear mixed models with a random intercept for each participant.

[a] Models were adjusted for child's age and sex, maternal age at enrollment, maternal educational level, maternal smoking during pregnancy, and child's secondhand smoke exposure.

[b] Models were adjusted for a generalized propensity score generated from child's age and sex, maternal age at enrollment, maternal educational level, maternal smoking during pregnancy, child's secondhand smoke exposure, housing type, distance from major roads, presence of nearby factories, presence of a nearby waste incineration plant, and birth order.

[c] Models were adjusted for child's age and sex, maternal age at enrollment, maternal educational level, maternal smoking during pregnancy, and child's secondhand smoke exposure, and were weighted using stabilized inverse probability weights derived from the generalized propensity scores.

markedly by sleep duration. Specifically, lead levels at ages 6, 8, and 10 years were associated with lower word, color, and color–word test scores at the same ages among children sleeping ≤ 8 h; with lower color test scores among those sleeping > 8 to < 10 h; and with no associations among those sleeping ≥ 10 h (Fig. 1 and Table S6). When formally tested using a lead × sleep duration interaction term in the mixed model, no statistically significant interaction was detected (all *p*-values for interaction > 0.40).

Our exploratory analyses revealed no consistent evidence of associations between blood lead levels and sleep duration, nor between sleep duration and SCWT scores. An exception was observed in the doubly robust model, where children sleeping 8–10 h (vs. ≤8 h) showed higher word test scores (Tables S7 and S8).

In the sensitivity analysis excluding adjustment for child's age and sex, and omitting these variables from the GPS model, the associations of lead levels with color and color–word test scores remained robust. Notably, an additional statistically significant association was observed for the word score, which had not been evident in the primary analysis (Table S9).

4. Discussion

In this study, based on an ongoing prospective birth cohort in Korea, we found evidence consistent with a causal association between blood lead levels and SCWT performance—particularly color and color–word test scores—among school-age children at ages 6, 8, and 10 years. These associations remained consistent across different causal inference approaches, including GPS adjustment and doubly robust estimation. Importantly, the associations were stronger among children sleeping ≤ 8 h than among those sleeping > 8 h.

Previous studies on lead exposure and selective attention have reported inconsistent findings (Choi et al., 2020; Kim et al., 2010; Schwartz et al., 2000; Surkan et al., 2007; Yu et al., 2019, 2021). In a cross-sectional study of Korean school-age children (mean age, 9.7 years) not overlapping with participants of this study, higher blood lead levels were associated with lower Stroop color–word test scores (Kim et al., 2010). A prospective study of U.S. former lead workers (mean age, 55.6 years; mean interval, 16.0 years since cessation of occupational exposure) reported that peak tibia lead was linked to accelerated declines in Stroop interference scores (Schwartz et al., 2000). By contrast, a cross-sectional study of U.S. children (mean age, 8.0 years) found no associations between blood lead levels and Stroop interference scores (Surkan et al., 2007). Likewise, two studies based on the same occupational cohort of newly hired U.S. lead workers found no cross-sectional or longitudinal associations between blood lead levels and SCWT scores (Yu et al., 2019, 2021). Another cross-sectional study of Korean children and adolescents observed no significant correlations between blood lead levels and Stroop word, color, or color–word test scores (all *p*-values > 0.15), although correlation coefficients were consistently negative (Choi et al., 2020). Because these earlier investigations largely relied on conventional observational designs that cannot fully exclude residual confounding, our findings—derived using multiple causal inference methods—provide more robust evidence that lead exposure impairs selective attention in school-age children.

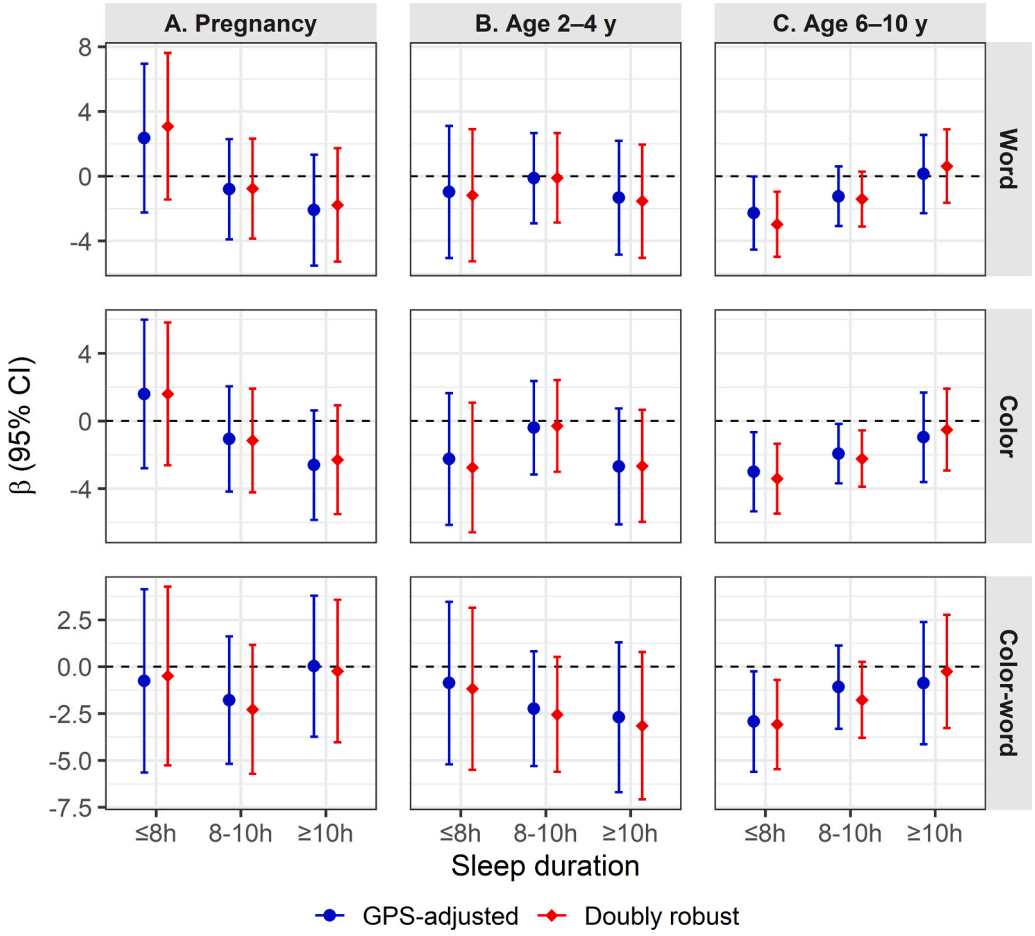

Fig. 1. Associations between blood lead concentrations measured during pregnancy (A), ages 2–4 years (B), and ages 6–10 years (C) and Stroop color and word test T-scores (Word, Color, and Color–Word) in children aged 6–10 years, stratified by sleep duration (≤8 h, 8–10 h, and ≥10 h). Blue circles with error bars indicate estimates and 95 % confidence intervals from linear mixed models adjusted for generalized propensity score and confounders, whereas red diamonds with error bars indicate estimates and 95 % confidence intervals from doubly robust models. The dashed horizontal line denotes the null values (β = 0).

Our findings indicate that lead levels were more consistently associated with lower Stroop color and color–word test scores than with word test scores, aligning in part with previous research that reported the associations between lead exposure and lower Stroop color–word test scores (Kim et al., 2010). This pattern may reflect the differing cognitive demands of the subtests: the word test primarily captures automatic processing speed, whereas the color test and especially the incongruent color–word test require greater working memory, conflict monitoring, and inhibitory control (Periáñez et al., 2021). Thus, the neurotoxic impact of lead may be concentrated on more demanding attentional and executive components of the task, with exposure potentially impairing frontal circuits involved in selective attention and conflict resolution.

In our cohort, prenatal blood lead concentrations (approximately, mid-pregnancy) were not associated with SCWT performance, whereas lead levels at ages 6, 8, and 10 years were linked to poorer scores. Because blood lead has a short half-life of < 30 days and primarily reflects recent exposure (Specht et al., 2019), blood lead levels at ages 6, 8, and 10 years likely capture ongoing neurotoxic effects occurring in close temporal proximity to Stroop testing. In contrast, any subtle neurodevelopmental effects of prenatal lead exposure may have been mitigated or masked by subsequent environmental influences and neural plasticity during the postnatal period.

In the present study, the associations between lead levels and lower SCWT scores were more pronounced among children sleeping ≤ 8 h than among those sleeping longer. Insufficient sleep may compromise the brain's restorative function, such as glymphatic clearance of neurotoxic metabolites, thereby increasing susceptibility to neurotoxic effects of lead (Eugene and Masiak, 2015). The glymphatic system, which facilitates metabolic clearance from the brain, is most active during deep sleep stages (Eugene and Masiak, 2015). Importantly, this potential biological interaction does not necessarily require a direct association between lead exposure and sleep duration or between sleep duration and SCWT scores. Instead, sleep duration may function as an effect modifier by altering the brain's capacity to tolerate or recover from neurotoxic insults, rather than acting as an independent risk factor. Alternatively, shorter sleep duration may serve as a marker of a subgroup inherently more vulnerable to the detrimental effects of lead, given that lead exposure itself has been linked to poorer sleep quality and reduced sleep duration (Jansen et al., 2019). In this context, sleep duration may reflect broader resilience-related characteristics, such as neurodevelopmental robustness, home environment, or psychosocial stress, that modify susceptibility to lead toxicity, even in the absence of a direct association with the outcome.

Although stratified analyses suggested stronger associations between blood lead levels and selective attention among children sleeping ≤ 8 h, formal tests for interaction using a lead $\times$ sleep duration term were not statistically significant. This likely reflects limited statistical power due to the small sample size in the ≤ 8-hour group, rather than definitive evidence against effect modification. The within-child correlation estimated from the mixed-effects models was relatively high (ICC $= 0.40$). Under the observed study design, simulation-based analyses indicated that the study did not achieve 80 % power to detect a lead $\times$ sleep interaction even for relatively large standardized effect sizes (up to approximately 0.34 SD per 1 SD increase in lead). This finding suggests that the interaction analyses were underpowered. These considerations indicate that the observed modification by sleep duration should be interpreted as hypothesis-generating rather than definitive. Although no prior studies have explicitly examined sleep duration as a modifier of lead's neurobehavioral effects, our findings suggest that promoting adequate sleep could be a practical approach to mitigating such risks and highlight the potential sleep-targeted interventions. Further research is warranted to confirm these findings and elucidate the underlying mechanisms.

In sex-stratified analyses, the associations between lead levels and SCWT scores—particularly color–word test scores—tended to be stronger among girls than boys. This pattern may reflect sex-related differences in susceptibility to neurotoxicants, potentially mediated by hormonal influences on brain development, differences in lead toxicokinetics, or variation in cognitive task engagement (Llop et al., 2013; Theppeang et al., 2008). Prior studies have also reported sex-specific patterns in lead neurotoxicity; for instance, a Korean birth cohort study found stronger associations between lead exposure at ages 2 and 5 years and behavioral problems at age 5 years among girls than boys (Joo et al., 2018). In addition, a scoping review concluded that females may be more vulnerable to postnatal lead exposure in terms of neurocognitive outcomes such as intelligent quotient, whereas lead-exposed boys may be at greater risk for externalizing behavior problems (Singh et al., 2018). Although these findings are consistent with our observations, the overlapping CIs in our study underscore the need for cautious interpretation and larger studies to determine whether sex modifies the neurobehavioral effects of lead.

Lead readily crosses the blood-brain barrier by mimicking Ca^{2+}, accumulating in the developing brain, where aberrant calcium signaling inappropriately activates calmodulin-dependent pathways, thereby disrupting synaptogenesis and synaptic plasticity (Goldstein, 1993). Lead also alters neurotransmitter systems by impairing dopaminergic transmission and reducing GABA-mediated inhibition (Needleman, 2004). In addition, lead induces mitochondrial dysfunction, triggers glutamate excitotoxicity, and delays myelination (Lidsky and Schneider, 2003). Collectively, these neurotoxic mechanisms hinder the maturation of prefrontal-striatal circuits critical for inhibitory control and sustained attention, providing a biological basis for the observed reductions in SCWT performance among children with higher lead levels.

The present study has several notable strengths. First, this study utilized data from a prospective birth cohort that followed children up to age 10, allowing for stronger temporal inference between exposures and outcomes. Second, we applied multiple causal inference approaches to evaluate the impact of lead exposure on selective attention. While these methods are increasingly used in other fields of epidemiology, their application within environmental epidemiology remains limited; to our knowledge, this is the first study to apply these methods to lead neurotoxicity. Third, blood lead concentrations were repeatedly measured during pregnancy and at 2, 4, 6, 8, and 10 years, improving the reliability of exposure assessment and allowing us to identify susceptible windows for adverse neurobehavioral outcomes. Fourth, SCWTs were administered repeatedly at ages 6, 8, and 10 years by trained clinical psychologists using a validated Korean version of the test, reducing the risk of outcome misclassification.

However, several limitations should also be acknowledged. First, although this study employed causal inference approaches such as GPS adjustment and doubly robust estimation, residual confounding from unmeasured factors cannot be entirely excluded. For example, information on parental cognitive ability, the quality of the home learning environment, and child nutritional status (e.g., iron deficiency), which have been associated with both exposure and neurocognitive outcomes, could not be considered in this study. Despite adjustment for a wide range of sociodemographic and environmental covariates and the application of doubly robust estimation, residual confounding by these unmeasured factors may have influenced the magnitude of the observed associations. Furthermore, causal interpretation of these findings relies on key assumptions inherent to observational causal inference methods, including the absence of unmeasured confounding, correct specification of the exposure and outcome models, and the validity of the positivity and consistency assumptions. These assumptions cannot be fully verified and should be considered when interpreting the results. Future research should consider alternative approaches more robust to unmeasured confounding, such as instrumental variable analysis and difference-in-differences methods (Angrist and Krueger, 2001; Goodman-Bacon, 2021). Second, while blood lead is the most widely used biomarker in epidemiological studies—especially in children—its short half-life limits its ability to reflect cumulative exposure. Prior studies in adults have

linked bone lead, a more stable marker of long-term exposure, with steeper annual declines in SCWT scores (Schwartz et al., 2000). Because blood lead primarily reflects recent exposure, the inability to account for cumulative lead burden may have resulted in an underestimation of the true neurotoxic effects of lead on selective attention. Therefore, the associations observed in the present study should be interpreted as conservative estimates of the impact of long-term lead exposure. In addition, this limitation has implications for the interpretation of sensitive exposure windows, as associations observed at specific ages may primarily reflect the effects of temporally proximal exposure rather than the cumulative impact of earlier lead burden. Thus, incorporating bone lead or other long-term biomarkers in future studies may provide a more refined characterization of chronic lead exposure. Third, because no previous studies have evaluated sleep duration as a modifier of the lead–selective attention relationship, our findings should be interpreted with caution. Furthermore, sleep duration was assessed using parent-reported questionnaires rather than objective measures such as actigraphy, which may have introduced misclassification bias. Such non-differential misclassification of sleep duration would be expected to attenuate true effect modification, suggesting that the observed differences by sleep duration may represent conservative estimates. Nevertheless, the possibility of residual misclassification contributing to spurious effect modification cannot be entirely excluded and should be considered when interpreting these findings. Replication in other cohorts and, importantly, intervention studies are needed to confirm whether adequate sleep mitigates lead-related neurobehavioral risks and to evaluate the effectiveness of sleep-targeted public health strategies. Fourth, the generalizability of these findings should be interpreted with caution, as this study was conducted among Korean children with relatively low blood lead concentrations. Nevertheless, the observed associations at low exposure levels may be relevant to other populations experiencing similar background lead exposure. Fifth, because stratification substantially reduced the sample size, particularly in the $\leq$ 8-hour sleep group, our study may have been underpowered to detect modest interaction effects, increasing the risk of Type II error. The lack of statistically significant interaction terms should not be interpreted as evidence against effect modification by sleep duration. Rather, the results reflect limited statistical power, particularly for detecting modest interaction effects, and the stratified findings should be interpreted as hypothesis-generating.

5. Conclusions

Blood lead concentrations were associated with poorer selective attention in school-age children, and the application of multiple causal inference approaches supports a potential causal relationship. Associations were stronger among children sleeping $\leq$ 8 h compared with those sleeping longer. By applying multiple causal inference approaches, this study provides more robust evidence for the neurotoxic effects of lead on selective attention than prior observational studies. However, these findings should be interpreted in light of the assumptions required for causal inference in observational data. Our findings also suggest that ensuring adequate sleep may serve as a practical strategy to mitigate such risks, highlighting the potential of sleep-targeted interventions. Future research should incorporate diverse causal inference methods, including approaches more robust to unmeasured confounding (e.g., instrumental variable analysis), and further assess sleep duration as a potential effect modifier through replication in other cohorts and intervention-based studies.

CRediT authorship contribution statement

Heeseon Jang: Conceptualization, Methodology, Writing – Original Draft. **Choong Ho Shin:** Methodology, Investigation, Writing – Review & Editing. **Young Ah Lee:** Methodology, Investigation, Writing – Review & Editing. **Yun Jeong Lee:** Methodology, Investigation, Writing – Review & Editing. **Youn-Hee Lim:** Methodology, Investigation, Writing – Review & Editing. **Yun-Chul Hong:** Methodology, Investigation, Writing – Review & Editing. **Bung-Nyun Kim:** Methodology, Investigation, Writing – Review & Editing. **Dong Wook Lee:** Methodology, Investigation, Writing – Review & Editing. **Johanna Inhyang Kim:** Methodology, Investigation, Writing – Original Draft, Supervision. **Kyoung-Nam Kim:** Conceptualization, Methodology, Software, Formal analysis, Writing – Original Draft, Visualization, Supervision.

Ethics statement

The Institutional Review Board of Seoul National University Hospital approved the study protocol (IRB No. 1201–010–392). The study adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from parents of all participants and additionally from children at ages 8 and 10 years.

Funding sources

This study was supported by the Ministry of Environment through the Environmental Health Center Program of the Republic of Korea. Additional support was provided by a grant from the Ministry of Food and Drug Safety (18162MFDS121), the research fund of Hanyang University (HY-202400000001017), and the Korea Environmental Industry & Technology Institute (KEITI) through the Core Technology Development Project for Environmental Diseases Prevention and Management Project, funded by the Korea Ministry of Environment (MOE) (RS-2022-KE002052).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We sincerely thank all the children and their parents for their participation in the Environment and Development of Children (EDC) study.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2026.119845.

Data availability

The data that has been used is confidential.

References

Angrist, J.D., Krueger, A.B., 2001. J. Econ. Perspect. 15, 69–85. https://doi.org/10.1257/jep.15.4.69.
Asaoka, S., Nishimura, R., Nozoe, K., Yamamoto, R., 2025. Sleep. Biol. Rhythms 23, 13–20. https://doi.org/10.1007/s41105-024-00546-9.
Austin, P.C., 2018. Stat. Med 37, 1874–1894. https://doi.org/10.1002/sim.7615.
Bang, H., Robins, J.M., 2005. Biometrics 61, 962–973.
Carrel, M., Zahrieh, D., Young, S.G., Oleson, J., Ryckman, K.K., Wels, B., Simmons, D.L., Saftlas, A., 2017. PLoS One 12, e0177930. https://doi.org/10.1371/journal.pone.0177930.
Choi, J.-W., Jung, A.-H., Nam, S., Kim, K.M., Kim, J.W., Kim, S.Y., Kim, B.-N., Kim, J.-W., 2020. BMC Psychiatry 20, 407. https://doi.org/10.1186/s12888-020-02799-3.
Eugene, A.R., Masiak, J., 2015. MEDtube Sci. 3, 35–40.
Fisher, A.V., 2019. Curr. Opin. Psychol. 29, 248–253. https://doi.org/10.1016/j.copsyc.2019.06.002.
Giffin, A., Reich, B.J., Yang, S., Rappold, A.G., 2023. Biometrics 79, 2220–2231. https://doi.org/10.1111/biom.13745.
Goldstein, G.W., 1993. Neurotoxicology, 14, 97–101.
Goodman-Bacon, A., 2021. J. Econ. 225, 254–277.

Jansen, E.C., Dunietz, G.L., Dababneh, A., Peterson, K.E., Chervin, R.D., Baek, J., O'Brien, L., Song, P.X.K., Cantoral, A., Hu, H., Téllez-Rojo, M.M., 2019. J. Clin. Sleep. Med 15, 1443–1449. https://doi.org/10.5664/jcsm.7972.

Joo, H., Choi, J.H., Burm, E., Park, H., Hong, Y.-C., Kim, Y., Ha, E.-H., Kim, Y., Kim, B.-N., Ha, M., 2018. Sci. Total Environ. 615, 1086–1092. https://doi.org/10.1016/j.scitotenv.2017.10.007.

Kim, K.-N., Lim, Y.-H., Shin, C.H., Lee, Y.A., Kim, B.-N., Kim, J.I., Hwang, I.G., Hwang, M.S., Suh, J.-H., Hong, Y.-C., 2018. Int J. Epidemiol. 47, 1049–1050f. https://doi.org/10.1093/ije/dyy070.

Kim, Y., Cho, S.-C., Kim, B.-N., Hong, Y.-C., Shin, M.-S., Yoo, H.-J., Kim, J.-W., Bhang, S.-Y., 2010. Sci. Total Environ. 408, 5737–5743. https://doi.org/10.1016/j.scitotenv.2010.07.070.

Lidsky, T.I., Schneider, J.S., 2003. Brain 126, 5–19. https://doi.org/10.1093/brain/awg014.

Llop, S., Lopez-Espinosa, M.-J., Rebagliato, M., Ballester, F., 2013. Toxicology 311, 3–12.

Needleman, H., 2004. Annu Rev. Med 55, 209–222. https://doi.org/10.1146/annurev.med.55.091902.103653.

Periáñez, J.A., Lubrini, G., García-Gutiérrez, A., Ríos-Lago, M., 2021. Arch. Clin. Neuropsychol. 36, 99–111. https://doi.org/10.1093/arclin/acaa034.

Pouliou, T., Sera, F., Griffiths, L., Joshi, H., Geraci, M., Cortina-Borja, M., Law, C., 2015. J. Epidemiol. Community Health 69, 77–85. https://doi.org/10.1136/jech-2014-204287.

Rabiner, D.L., Godwin, J., Dodge, K.A., 2016. Sch. Psychol. Rev. 45, 250–267.

Schwartz, B.S., Stewart, W.F., Bolla, K.I., Simon, P.D., Bandeen-Roche, K., Gordon, P.B., Links, J.M., Todd, A.C., 2000. Neurology 55, 1144–1150. https://doi.org/10.1212/wnl.55.8.1144.

Shin, M.S., Park, M.J., 2007. Stroop Color and Word Test: A Manual for Clinical and Experimental Uses. Hakjisa, Seoul.

Singh, G., Singh, V., Sobolewski, M., Cory-Slechta, D.A., Schneider, J.S., 2018. Front Genet 9, 89. https://doi.org/10.3389/fgene.2018.00089.

Song, T., Xu, L., Peng, Z., Wang, L., Dai, C., Xu, M., Shao, Y., Wang, Y., Li, S., 2023. Cogn. Neurodyn 17, 621–631. https://doi.org/10.1007/s11571-022-09861-8.

Specht, A.J., Weisskopf, M., Nie, L.H., 2019. J. Expo. Sci. Environ. Epidemiol. 29, 416–423. https://doi.org/10.1038/s41370-018-0036-y.

Stevens, C., Bavelier, D., 2012. Dev. Cogn. Neurosci. 2 (1), S30–S48. https://doi.org/10.1016/j.dcn.2011.11.001.

Surkan, P.J., Zhang, A., Trachtenberg, F., Daniel, D.B., McKinlay, S., Bellinger, D.C., 2007. Neurotoxicology 28, 1170–1177. https://doi.org/10.1016/j.neuro.2007.07.007.

Takeuchi, H., Taki, Y., Nouchi, R., Yokoyama, R., Kotozaki, Y., Nakagawa, S., Sekiguchi, A., Iizuka, K., Hanawa, S., Araki, T., Miyauchi, C.M., Sakaki, K., Nozawa, T., Ikeda, S., Yokota, S., Daniele, M., Sassa, Y., Kawashima, R., 2021. Commun. Biol. 4, 912. https://doi.org/10.1038/s42003-021-02435-0.

Tandon, P.S., Zhou, C., Sallis, J.F., Cain, K.L., Frank, L.D., Saelens, B.E., 2012. Int J. Behav. Nutr. Phys. Act. 9, 88. https://doi.org/10.1186/1479-5868-9-88.

Taylor, C.M., Golding, J., Hibbeln, J., Emond, A.M., 2013. PLoS One 8, e72371. https://doi.org/10.1371/journal.pone.0072371.

Theppeang, K., Glass, T.A., Bandeen-Roche, K., Todd, A.C., Rohde, C.A., Schwartz, B.S., 2008. Am. J. Public Health 98, 1248–1255. https://doi.org/10.2105/AJPH.2007.118505.

Wiggins, E., Mottarella, M., Good, K., Eggleston, S., Stevens, C., 2018. Neurosci. Lett. 677, 32–36. https://doi.org/10.1016/j.neulet.2018.04.022.

Yu, C.-G., Yang, W.-Y., Saenen, N., Wei, F.-F., Zhang, Z.-Y., Mujaj, B., Thijs, L., Feng, Y.-M., Nawrot, T.S., Staessen, J.A., 2019. Scand. J. Work Environ. Health 45, 298–307. https://doi.org/10.5271/sjweh.3798.

Yu, Y.-L., Thijs, L., Saenen, N., Melgarejo, J.D., Wei, D.-M., Yang, W.-Y., Yu, C.-G., Roels, H.A., Nawrot, T.S., Maestre, G.E., Staessen, J.A., Zhang, Z.-Y., 2021. Scand. J. Work Environ. Health 47, 233–243. https://doi.org/10.5271/sjweh.3940.

Ziegeldorf, A., Schoene, D., Fatum, A., Brauer, K., Wulff, H., 2024. BMC Public Health 24, 2247. https://doi.org/10.1186/s12889-024-19174-6.