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Secondhand Tobacco Smoke Exposure and Neuromotor Function in Rural Children

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Abstract

Objectives—To investigate the relationship between secondhand tobacco smoke (SHS) exposure and neuromotor function in children.

Study design—We studied 404 children aged 7–9 years who were exposed to SHS and other environmental neurotoxicants. Parent reported smoking habits, and serum cotinine levels were measured in children to determine SHS exposure. Halstead-Reitan Finger Oscillation Test (HRFOT), Purdue Grooved Pegboard Test – Kiddie version (PGPT), and Bruininks-Oseretsky Test of Motor Proficiency 2-Short form (BOT-2) were used to assess neuromotor function. Multivariable regression models that accounted for potential confounders were used to evaluate the associations.

Results—Approximately 50% of the children were exposed to SHS based on serum cotinine measures. Exposure to SHS was significantly associated with motor impairment in children, including diminished visuo-motor coordination (p=0.01), fine motor integration (p=0.01), balance (p=0.02), and strength (p=0.04) after adjusting for exposures to lead and manganese, age, sex,

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body mass index, measures of cognitive abilities of parents, parental education, and quality of home environment

Conclusions—We conclude that SHS is a neurotoxicant that may be associated with impaired childhood neuromotor function.

Keywords

children; cotinine; exposure; passive smoking; motor tests

There is compelling evidence from several studies supporting the association between secondhand tobacco smoke (SHS) exposure and increased risk of learning disabilities,(1–3) attention-deficit/hyperactivity disorder (ADD/ADHD),(2–10) behavior and conduct disorders,(3–5, 9, 10) and cognitive and academic achievement deficits in children.(11–14) There is little research, however, on the effects of tobacco smoke exposure on neuromotor function, an important component of neuropsychological function, which is related to overall cognitive attainment and achievement in clinical pediatric populations(15) as well as typically developing children.(16, 17) Indeed, there is strong evidence from research on children with developmental disorders and emerging evidence from typically developing children, that motor skills and cognitive abilities are interrelated at the behavioral(15, 18–26) and neuroanatomical level.(16, 17, 27)

Of the few studies examining the role of prenatal tobacco smoke exposure on motor development in children at different ages, results have been equivocal. Trasti et al found a small, but significant negative association between maternal smoking during pregnancy and motor development in children at age 5 years.(33) Barr et al found a significant relationship between prenatal exposure to tobacco and lower examiner ratings on fine and gross motor skills in children at age 4 years. After adjusting for significant outliers (subjects reporting > 3 ½ cigarettes/day) and other covariates such as parental education, prenatal nutrition, maternal age, race, and use of other drugs, however, evidence of a relationship did not persist.(34) Other studies by Richardson et al,(35) and Fried and Watkinson(36) observed similar non-significant associations between prenatal exposure to tobacco smoke and impaired motor development in children. Hernandez-Martinez et al observed that neonates (48–72 hours old) of mothers, who smoked during pregnancy or were exposed to SHS based on self-reported measures, had significantly lower scores on motor performance, quality of movement, and muscular tone.(37)

Motor skills are essential in children’s daily activities with long-term consequences for their cognitive and socio-emotional development. Nevertheless, there is a conspicuous gap in the literature on SHS exposure and its role on neuromotor function in children. Therefore, the aim of the current study was to assess the relationship between SHS exposure and neuromotor function in 7–9 year old children enrolled in an investigation of environmental exposures.

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METHODS

The data for this study were drawn from the Communities Actively Researching Exposure Study (CARES), a community-based participatory research study of 404 children and their families. The study was designed to answer the community's primary research question, "Does manganese in our air affect our children's health?" (38) The study took place in Marietta, Ohio, the home of the longest-running ferromanganese refinery in North America(39). Children of families residing in the areas of Marietta and Cambridge, Ohio, and Vienna and Boaz, West Virginia were recruited for participation using a volunteer sampling strategy. Eligibility for the CARES study included children ages 7, 8, and 9 years and their families who resided in the catchment areas throughout their life with no plans to move for at least one year. In addition, their biological mother must have resided in the catchment area during her pregnancy with the child. Recruitment letters were sent home through schools, and advertisements were aired on local radio and printed in local newspapers. All participants signed informed consent and assent forms approved by the Institutional Review Board of the University of Cincinnati. Study participants were enrolled from 2009 through 2013.

Measurement of Neuromotor Outcomes and SHS Exposure

Three neuromotor tests assessing fine motor and gross motor development, and visual motor skills were utilized: (1) Halstead-Reitan Finger Oscillation Test (HRFOT); (2) Purdue Grooved Pegboard Test – Kiddie version (PGPT); and (3) Bruininks-Oseretsky Test of Motor Proficiency 2 - Short form (BOT-2). These instruments were selected because of their proven psychometric properties with respect to the assessment of gross and fine motor skills in pediatric populations (40). Neuromotor assessment in children was completed by a trained examiner, blinded to participants' exposure status, in a standardized testing situation. Before administering the tests, each participant was asked to write any word on paper, toss a tennis ball with one hand, and kick a ball to determine their dominant and non-dominant hand and leg.

HRFOT is a test of simple motor speed and is part of the Halstead-Reitan Neuropsychological Test Battery.(41, 42) In this test, the participant taps on a finger tapper board as fast as possible with his/her index finger, with the tapping motion occurring only at the index finger joint and not at the wrist or forearm. The test was evaluated separately for dominant and non-dominant hands. The test includes five trials of 10 second each, with a 15-second rest period between each trial and 2-minute rest period after the first two trials. Average number of taps from the five trials, for each hand, was the measured outcome. PGPT is a test of manual dexterity requiring complex visuo-motor coordination. A standard grooved pegboard apparatus (Lafayette instruments # 32025) of dimensions 10.1 cm x 10.1 cm metal surface, with a 5 x 5 matrix of keyhole-shaped holes in varying orientations was used. For the kiddie version we used a 2 x 5 matrix for a total of 10 holes. Each participant was required to match the groove of the peg, which contains a round side and a square side, with the groove of the peg board containing similar round and square holes as quickly as possible using one peg and one hand at a time. The test was evaluated separately for dominant and non-dominant hands. Participants had to place the peg on the board from a left

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to right direction when using their right hand and right to left when using their left hand. In addition to directionality, the top row must be filled first, followed by the bottom row. Time to complete the task, for each hand, was the measured outcome.

The BOT-2, a revision of the Bruininks-Oseretsky Test of Motor Proficiency,(43) is a test designed to measure several fine and gross motor skills. For our study, we used BOT-2 short form comprising 14 test items measuring eight motor functions, which yields four motor area standardized composite T scores (Mean=50; SD=10) and a total motor composite age-standardized T score (Mean=50; SD=10)

Children's exposure to SHS was assessed using parent self-reported smoking habits and measurement of the child' s serum cotinine level. A child was considered exposed to SHS if a household member reported smoking ≥ 1 cigarette/day or his serum cotinine level was ≥ 0.05 ng/mL. A parent or legal guardian from each participating household in the study provided information on the number of individuals residing in their household, relationship to the child, and number of cigarettes smoked per day, if any. Serum cotinine levels were determined by the New York State Department of Health's (NYS DOH) Wadsworth Center, Division of Environmental Health Sciences in Albany, New York using a high throughput 96-well plate format sample preparation, and then analyzed using an isotope dilution, liquid chromatography/tandem mass spectrometry (LC/MS/MS) method. The method used is a modification of techniques used by the Centers for Disease Control and Prevention for the National Health and Nutrition Examination Survey (NHANES)(44) and New York State Wadsworth Laboratories for the NYC NHANES studies.(45) Each serum specimen was equilibrated with a trideuterated cotinine internal standard solution and extracted using a 96-well Bond Elut Plexa Solid Phase Extraction (SPE) plate (Varian, Palo Alto, CA). The acetonitrile sample extract was taken to dryness, reconstituted in 96%/4% acetonitrile/water solution, and analyzed by LC/MS/MS using electrospray ionization. The instrumental systems comprised a Shimadzu Prominence LC with a Phenomonex Luna Hilic (100 x 2.00 mm) column and an AB Sciex API 4000 triple quadrupole mass spectrometer operated in ESI positive ion mode using multiple reaction monitoring (MRM) detection. Three QC pools were used at low, medium, and high target cotinine concentrations of 0.173, 1.61 and 15.7 ng/mL. Final results were blank corrected using the mean batch blank value. The method detection limit (MDL) for this method was 0.05 ng/mL cotinine in serum.

Approximately 51% (n = 162) of the samples in our study were below the MDL; however, the lab reported actual values for samples below this reporting limit of detection, and we used those values in our statistical analyses. Approximately 84% (n = 340) of the children consented to provide blood samples. Among these consented subjects, blood could not be drawn in 3% (n=13), and the sample's serum could not be extracted in 1% (n=4).

Covariates

Several covariates and confounders known potentially to influence the association between SHS exposure and neurobehavioral outcomes were measured. Demographic factors including child's age (years), sex, race, height ,and weight were ascertained by the study's research assistant. The child's body mass index (BMI, weight in kilograms/height in meter-squared) was ascertained from Centers for Disease Control's defined BMI-for-age growth

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charts for girls and boys was obtained. Information on prenatal smoking (yes/no), parent intelligence quotient (IQ) from the two subtest version (vocabulary and matrix reasoning) of Wechsler Abbreviated Scale of Intelligence (WASI),(46) education level of the primary caregivers as an index of socioeconomic status based on the Barratt Simplified Measure of Social Status (BSMSS),(47) and multiple dimensions of the home rearing environment relevant to the child's neurobehavioral development using the Parenting Relationship Questionnaire (PRQ)(48) were collected. In addition, biomarkers of metal exposure such as blood lead (BPb, μg/dL), blood manganese (BMn, μg/L) and hair Mn (HMn, ng/g) known to have adverse effects on the central nervous system were included in the analysis. Analytical procedures estimating BPb, BMn, and HMn concentrations are described in detail elsewhere.(49)

Statistical Analyses

Demographic characteristics and biomarkers of environmental exposure are presented as means (± SD) or medians (interquartile range, IQR) for continuous variables and by frequencies (percentages) for discrete variables as appropriate. Because the distribution of serum cotinine level and other environmental toxicant measurements were skewed, we applied natural logarithmic transformation to the raw data. Multivariable linear regression modeling with a backward stepwise procedure was used to identify variables that were significant at an *a priori* alpha value of 0.05.

We started our analysis by examining the bivariate association between each neuromotor outcome, and serum cotinine and other covariates respectively. Given that the BOT-2 Total Motor Composite score was constructed from total point scores of eight subtests, we planned to conduct a secondary analysis to determine which subtests were significantly associated with serum cotinine levels and other neurotoxicants if the overall BOT-2 index score was significantly associated with serum cotinine. Variables that were significant at $p<0.25$ were included in the initial multivariable analyses. Biologically pertinent 2-way interactions were entertained in the initial multivariable model to identify potential effect modifiers of the association between serum cotinine and the outcomes. Quadratic terms for BMn and HMn were examined in the models due to the documented evidence of a nonlinear association between Mn exposure and childhood neurodevelopment.(50) Additionally, a change in the regression estimate of ≥ 10% for serum cotinine during the backward elimination procedure was considered a confounding effect, and retained in the final model irrespective of its *p*-value. Adjusted regression estimates (β) and corresponding 95% confidence intervals are reported. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC).

RESULTS

A total of 404 children participated in the study. Descriptive characteristics of the study cohort and biomarkers of environmental exposure variables are presented in Table I. Fifty-four percent of the children were boys, and 95% Caucasian. Thirty-seven percent of the children were exposed to a median of 20 cigarettes per day per household as reported by parents, and 50% of the children were exposed to SHS based on serum cotinine levels. The

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geometric mean serum cotinine, BPb and BMn values for children in our cohort were 0.08 ng/mL, 0.81 μg/dL, and 9.69 μg/L, respectively (Table I).

In bivariate analyses, the associations between the logarithmic transformation of serum cotinine levels and children's neuromotor performance on all the five neuromotor outcomes were statistically significant. BPb level showed a similar statistically significant association with dominant and non-dominant hand HRFOT, non-dominant hand PGPT, and BOT-2 total motor composite score outcome (Table II). There were no statistically significant associations between BMn and HMn concentrations with the neuromotor outcomes.

In multivariable analyses we found higher serum cotinine levels were significantly associated with higher scores on non-dominant hand PGPT, i.e. taking more time to complete a task (p=0.01) and lower scores on BOT-2 tests (p=0.009). We found a covariate-adjusted relationship between the log of serum cotinine and BOT-2 scores which indicated that an increase in the log serum cotinine from 1 to 10 ng/mL was associated with a 6.6 point decrease in BOT-2 score, a reduction of more than one-half of the SD score. Among the other environmental toxicants affecting neuromotor performance in children, we observed a significant non-linear relationship between BMn levels and non-dominant hand HRFOT (p=0.02) and BOT- 2 tests (p=0.005). Significantly lower scores on dominant (p=0.05) and non-dominant (p=0.003) hand HRFOT were also observed with higher BPb levels (Table III). The purpose of our BOT-2 subtest analyses was to determine which subtests were significantly associated with serum cotinine levels and other neurotoxicants. After adjusting for covariates that were associated with BOT-2 subtests, we found higher serum cotinine levels were significantly associated with lower scores on fine motor integration (β=-0.09, p=0.01), balance (β=-0.07, p (=0.02), and strength (β =- 0.14, p=0.04). The nonlinear relationship between BMn levels and BOT-2 subtests continued, with higher and lower BMn levels significantly associated with lower scores on fine motor precision (p=0.04), manual dexterity (p=0.002), balance (p=0.01), running speed (p=0.006), and strength (p=0.005), respectively (Table IV; available at www.jpeds.com). There were no significant interactions between serum cotinine level and BPb, BMn, or HMn.

Several covariates remained in our final multivariable models because of their association with neuromotor outcomes or their affected change on the regression coefficient for serum cotinine levels. Increasing age was significantly associated with better performance on all the neuromotor tests, except balance. There was no cotinine level-sex interaction observed. However, boys completed a greater number of taps on HRFOT; girls performed better on fine motor precision, fine motor integration, manual dexterity, bilateral coordination, balance, and running speed tests.

DISCUSSION

In this cross-sectional study examining the relationship between SHS exposure and neuromotor function in children, we found exposure to SHS was significantly associated with poor fine motor and gross motor development. In unadjusted analyses, SHS exposure was associated with poorer performance on tests of fine motor skills (HRFOT), visuo-motor coordination (PGPT), and fine and gross motor skills (BOT-2). After adjusting for other

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neurotoxicants and several covariates, SHS exposure was negatively associated with visuo-motor coordination, fine motor integration, balance, and strength. These findings have implications not only for individuals, but for the large number of children in the population who are exposed to SHS.(51)

The relationship between tobacco smoke exposure and childhood neuromotor function has been previously explored, but limited mostly to prenatal smoking. We instead examined the relationship between SHS exposure, using serum cotinine as a biomarker of SHS exposure, and childhood neuromotor function using a comprehensive battery of robust neuromotor tests. Findings from our study are similar to that of Trasti et al, who found that children of mothers who smoked during pregnancy had lower scores on balance and fine motor coordination (eye-hand coordination) at age five years compared with children of mothers who were non-smokers. The authors found a significant dose-response relationship between number of cigarettes smoked during pregnancy and children's scores on balance performance and fine motor coordination using the Peabody Developmental Motor Scales test.(33) Hernandez- Martinez et al also observed an inverse association between maternal exposure to SHS and their newborns scores on a motor system evaluation; (37) however, the small sample size (n=17) of that study, maternal self-report of SHS, and age at which neuromotor functions were assessed limit the comparison of their study findings.

Inclusion of other known neurotoxicants is a strength of the current investigation. Neurotoxicological studies have clearly established the association between low-level Pb exposure (BPb < 10μg/dL) and motor deficits in children. Studies have shown BPb levels of 9μg/dL are associated with motor dysfunctions in children such as upper-limb speed, dexterity, bilateral coordination, and visuo-motor ability.(52) Children from our cohort demonstrated poor upper limb coordination at geometric mean BPb levels as low as 0.81μg/dL after adjusting for other covariates. Evidence of neurotoxicant effects of Mn on children is emerging. A recent study by Lucchini et al, reported BMn and HMn levels were positively associated with increased resting tremor intensity.(53) Two other studies by Hernandez-Bonilla et al,(54) and Takser et al,(55) reported children exposed to Mn performed poorly on manual dexterity, fine motor coordination, and hand skill tests. Children in our cohort showed a characteristic non-linear association between BMn levels and fine motor precision, manual dexterity, balance, running speed, and strength, suggesting that both low and high manganese levels may have adverse effects on neuromotor function in children. A similar phenomenon of non-linear association was observed by Henn et al between Bayley Mental Development Index scores and BMn-levels at 12-months of age in a cohort of children born in Mexico City.(50)

Our results suggest that SHS exposure may be associated with childhood neuromotor deficits. Yet, the co-existence of multiple co-exposures and their effect on childhood neuromotor functions cannot be ruled out. Findings from our study that add strength to the neurotoxicant role of SHS are: (1) adjusting for the effects of concomitant neurotoxicants in the final multivariable models and still finding a significant negative associations; (2) lack of significant interaction between serum cotinine levels and other neurotoxicants; (3) use of serum cotinine as a biological measure of SHS exposure in examining the association and

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thus reducing recall bias; and (4) findings from our study that are consistent with neurotoxic effects observed in animal studies.(56, 57)

Our study has several limitations. The cross-sectional nature of the study design limits our study results to be interpreted as associational and not causal. Although serum cotinine offsets several limitations compared with self-report surveys, information on location of smoking and duration of exposure was not obtained. We did not distinguish the effects of prenatal tobacco smoke exposure from childhood SHS exposure in our analyses. Approximately 23% of the mothers in our study self-reported to smoking throughout pregnancy. Because prenatal exposure to smoking was not assessed by serum cotinine levels, we did not include it in the analyses. Nevertheless, residual confounding from prenatal tobacco smoke exposure cannot be ignored. A major strength of our study remains the covariates included in the analyses known to affect childhood neuromotor outcomes, such as measures of cognitive abilities of parents, quality of the home environment, and exposure to other environmental neurotoxicants.

Overall, the findings of this study indicate that SHS exposure may play a role in the development of childhood neuromotor function on an individual and population level. Children exposed to SHS have poorer fine motor, gross motor, and visuo-motor skills. Future research is needed to confirm these findings and if these neuromotor function deficits continue to persist in adolescence. Results from our study reinforce the importance of continued interventions to reduce childhood exposure to SHS.

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Abbreviations

CARES	Communities Actively Researching Exposure Study
HRFOT	Halstead-Reitan Finger Oscillation Test
PGPT	Purdue Grooved Pegboard Test (Kiddie version)
BOT-2	Bruininks-Oseretsky Test of Motor Proficiency 2 - Short form
SHS	Secondhand Smoke Exposure
BSMSS	Barratt Simplified Measure of Social Status
WASI	Weschler Abbreviated Scales of Intelligence
PRQ	Parenting Relationship Questionnaire

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Table 1

Demographic Characteristics of the Study Cohort

Characteristics	*N*	
Child Measures		
Age, mean ± SD, y	404	8.4 ± 0.9
Sex, *n* (%)	404	
Male		217 (53.7)
Female		187 (46.3)
Race, *n* (%)	404	
Caucasian[a]		379 (93.8)
Hispanic[b]		6 (1.5)
Other		19 (4.7)
Body Mass Index, mean ± SD	404	18.7 ± 3.9
Parent Measures		
Parent education, *n* (%)	398	
High school graduate or less		101 (33.9)
Any college		245 (61.2)
Postgraduate		52 (13.1)
Barratt's Education[c], mean ± SD	402	14.8 ± 2.5
Parent IQ, mean ± SD	404	104.8 ± 13.5
Parent self-reported smoking, *n* (%)	404	
Yes		148 (36.6)
No		256 (63.4)
No. of smokers/household, *n* (%)	148	
1		101 (25.0)
2–3		47 (11.6)
No. of cigarettes smoked/day/household, median (IQR)	148	20.0 (10.0, 30.0)
Maternal smoking during pregnancy, *n* (%)	391	
None		317 (81.1)
Throughout pregnancy		74 (23.3)
Biomarkers of Environmental Exposures		
Serum cotinine levels, ng/mL	329	
Geometric mean (95% CI)		0.08 (0.07, 0.10)
≥ 0.05 ng/mL		163 (49.5)
< 0.05 ng/mL		166 (50.5)
Blood lead levels, Geometric mean (95% CI), (μg/dL)	325	0.81 (0.77, 0.86)
Blood manganese levels, Geometric mean (95% CI), (μg/L)	325	9.69 (9.44, 9.94)
Hair manganese levels, Geometric mean (95% CI), (ng/g)	370	416.51 (380.15, 456.35)

[a] Non-Hispanic white;

[b] Hispanic ethnicity regardless of race.

[c] Barratt's education – measured as a weighted average of education level of parents and primary caregivers.

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Table 2

Bivariate Associations (Pearson correlations *r*) between Logarithmic of Serum Cotinine, BPb, BMn, HMn Levels and Children's Neuromotor Performance

	Serum Cotinine	BPb	BMn	HMn	Dominant hand HRFOT	Non-dominant hand HRFOT	Dominant hand PGPT	Non-dominant hand PGPT	BOT-2
Serum Cotinine									
BPb	0.35##								
BMn	−0.09	−0.12*							
HMn	0.25##	0.22#	0.001						
Dominant hand HRFOT	−0.14*	−0.18**	0.01	−0.10					
Non-dominant hand HRFOT	−0.19#	−0.21#	−0.02	−0.03	0.69##				
Dominant hand PGPT	0.20#	0.10	−0.04	0.07	−0.26##	−0.25##			
Non-dominant hand PGPT	0.20#	0.14*	0.03	0.04	−0.33##	−0.36##	0.64##		
BOT-2	−0.22##	−0.02	−0.03	−0.03	0.20#	0.24##	−0.25##	−0.26##	

* $p < 0.05$.

** $p < 0.01$.

\# $p < 0.001$.

\#\# $p < 0.0001$.

HRFOT- Halstead-Reitan Finger Oscillation Test.

PGPT - Purdue Grooved Pegboard Test – Kiddie version.

BOT-2 - Bruininks-Oseretsky Test of Motor Proficiency 2 (Short form), Total Motor Composite Score.

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Table 3

Multivariable Associations between Logarithmic of Serum Cotinine Levels and Children's Neuromotor Performance

Neuromotor Outcomes	Explanatory Variables	β (95% CI)	*P*	Adj. R^2
Dominant hand HRFOT	Serum cotinine	−0.19 (−0.54, 0.14)	0.25	
	Age	2.52 (1.81, 3.24)	<0.0001	
	Gender[a]	1.61 (0.30, 2.92)	0.02	0.18
	BPb	−1.50 (−3.03, 0.03)	0.05	
	Hair Mn	−0.49 (−1.27, 0.28)	0.21	
Non-dominant hand HRFOT	Serum cotinine	−0.26 (−0.57, 0.04)	0.09	
	Age	2.57 (2.00, 3.13)	<0.0001	
	Gender	2.86 (1.83, 3.89)	<0.0001	
	Barratt's Education	0.12 (−0.11, 0.36)	0.30	0.31
	BPb	−1.97 (−3.16, −0.77)	0.003	
	BMn (Linear)	35.29 (4.14, 66.44)	0.02	
	BMn (Quadratic)	−7.87 (−15.09, −1.19)	0.02	
Dominant hand PGPT	Serum cotinine	0.41 (−0.15, 0.97)	0.15	
	Age	−4.17 (−5.22, −3.13)	<0.0001	
	BMI	0.32 (0.05, 0.60)	0.02	0.21
	Barratt's Education	−0.33 (−0.77, 0.11)	0.14	
	BMn (Linear)	0.78 (−3.10, 4.66)	0.69	
	HMn (Linear)	0.24 (−0.84, 1.32)	0.65	
Non-dominant hand PGPT	Serum cotinine	0.71 (0.16, 1.26)	0.01	
	Age	−3.95 (−5.01, −2.90)	<0.0001	
	Barratt's Education	−0.34 (−0.79, 0.10)	0.13	0.19
	BMn (Linear)	2.90 (−1.11, 6.91)	0.16	
BOT-2, Total Motor Composite Score	Serum cotinine	−0.64 (−1.13, −0.16)	0.009	
	BMI	−0.44 (−0.69, −0.20)	0.003	
	Barratt's Education	0.33 (−0.05, 0.71)	0.09	
	BPb	1.18 (−0.71, 3.07)	0.22	0.15
	Blood Mn (Linear)	69.61 (20.80, 118.43)	0.005	
	Blood Mn (Quadratic)	−15.63 (−26.41, −4.85)	0.004	

[a] Gender: Reference group is female.

HRFOT: Halstead-Reitan Finger Oscillation Test.

PGPT: Purdue Grooved Pegboard Test – Kiddie version.

BOT-2: Bruininks-Oseretsky Test of Motor Proficiency 2 -Short form

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Table 4

Multivariable Associations between Logarithmic of Serum Cotinine Levels and BOT-2 Subtests.

BOT-2 Subtests	Explanatory Variables	β (95% CI)	*P*	Adj. R^2
Fine motor precision	Serum cotinine	−0.09 (−0.22, 0.05)	0.21	
	Age	0.70 (0.46, 0.94)	<0.0001	
	Gender	−1.14 (−1.58, −0.70)	<0.0001	
	Barratt's Education	0.10 (−0.002, 0.20)	0.05	
	Blood Pb	−0.32 (−0.83, 0.18)	0.21	0.24
	BMn (Linear)	13.80 (0.85, 26.75)	0.04	
	BMn (Quadratic)	−3.07 (−5.92, −0.21)	0.03	
	HMn (Linear)	0.001 (−0.26, 0.26)	0.99	
Fine motor integration	Serum cotinine	−0.09 (−0.17, −0.02)	0.01	
	Age	0.22 (0.08, 0.36)	0.002	
	Gender	−0.32 (−0.57, −0.07)	0.01	0.10
	Barratt's Education	0.02 (−0.03, 0.08)	0.40	
	HMn (Linear)	0.02 (−0.13, 0.17)	0.80	
Manual dexterity	Serum cotinine	−0.04 (−0.11, 0.03)	0.26	
	Age	0.54 (0.40, 0.67)	<.0001	
	Gender	−0.32 (−0.56, −0.08)	0.01	
	BMI	−0.02 (−0.05, 0.02)	0.36	
	Parent IQ	0.003 (−0.01, 0.01)	0.51	0.24
	BPb	0.06 (−0.23, 0.34)	0.69	
	BMn (Linear)	11.10 (4.02, 18.18)	0.002	
	BMn (Quadratic)	−2.44 (−4.00, −0.88)	0.002	
	HMn (Linear)	1.72 (0.39, 3.04)	0.01	
	HMn (quadratic)	−0.14 (−0.25, −0.03)	0.01	
Bilateral coordination	Serum cotinine	−0.03 (−0.09, 0.04)	0.40	
	Age	0.31 (0.19, 0.43)	<0.0001	
	Gender	−0.32 (−0.54, −0.11)	0.003	0.18
	Barratt's Education	0.10 (0.05, 0.15)	<0.0001	
	HMn (Linear)	0.06 (−0.07, 0.18)	0.37	
Balance	Serum cotinine	−0.07 (−0.13, −0.01)	0.02	
	Gender	−0.23 (−0.43, −0.03)	0.04	
	BMI	−0.04 (−0.07, −0.01)	0.003	
	Barratt's Education	−0.04 (−0.08, 0.01)	0.13	0.08
	Blood Mn (Linear)	7.48 (1.57, 13.39)	0.01	
	Blood Mn (Quadratic)	−1.66 (−2.96, −0.36)	0.01	
	Hair Mn (Linear)	0.08 (−0.03, 0.20)	0.16	
Running speed	Serum cotinine	−0.03 (−0.13, 0.07)	0.57	
	Age	0.26 (0.08, 0.44)	0.006	
	BMI	−0.11 (−0.16, −0.06)	<0.001	
	Parent IQ	−0.004 (−0.02, 0.01)	0.52	

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BOT-2 Subtests	Explanatory Variables	β (95% CI)	*P*	Adj. R^2
	Barratt's Education	0.03 (−0.06, 0.12)	0.49	0.13
	Blood Pb	0.05 (−0.33, 0.43)	0.79	
	Blood Mn (Linear)	13.44 (3.88, 22.99)	0.006	
	Blood Mn (Quadratic)	−3.04 (−5.14, −0.93)	0.004	
	Hair Mn (Linear)	1.20 (−0.58, 2.99)	0.19	
	Hair Mn (Quadratic)	−0.09 (−0.24, 0.05)	0.19	
Upper limb coordination	Serum cotinine	−0.12 (−0.31, 0.06)	0.19	
	Age	1.03 (0.70, 1.36)	<.0001	
	Barratt's Education	0.09 (−0.05, 0.23)	0.19	0.15
	Blood Pb	0.83 (0.14, 1.53)	0.02	
	Hair Mn (Linear)	0.26 (−0.09, 0.61)	0.15	
Strength	Serum cotinine	−0.14 (−0.28, −0.001)	0.04	
	Age	1.15 (0.88, 1.42)	<.0001	
	BMI	−0.14 (−0.22, −0.07)	0.001	
	Parent IQ	0.007 (−0.01, 0.03)	0.44	0.25
	BPb	0.22 (−0.35, 0.80)	0.45	
	Blood Mn (Linear)	20.63 (6.16, 35.10)	0.005	
	Blood Mn (Quadratic)	−4.60 (−7.79, −1.41)	0.005	
	Hair Mn (Linear)	0.21 (−0.07, 0.50)	0.14	