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Nonverbal Reasoning in Preschool Children: Investigating the Putative Risk of Secondhand Smoke Exposure and Attention-Deficit/Hyperactivity Disorder as a Mediator

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Abstract

Background: Exposure to secondhand smoke (SHS) has been found to be associated with cognitive deficits in children. However, relatively little is known about the relationship between SHS exposure, cognitive deficits, and smoking-related psychopathology, specifically attention-deficit/hyperactivity disorder (ADHD) and externalizing disorders such as conduct disorder (CD) and oppositional defiant disorder (ODD) in preschool children.

Methods: Children (n = 54) between the ages of 4 and 6 years from a comprehensive, longitudinal study of preschool emotional development were included in this study. Each child's primary caregiver completed questionnaires and interviews related to childhood psychopathology. SHS exposure was estimated with the use of saliva cotinine values.

Results: After adjustment for sociodemographic factors (e.g., age, gender, an income-to-needs ratio) and for ADHD, CD, and ODD symptoms, exposure to SHS was found to be negatively associated with preschool children's nonverbal reasoning skills. Exposure to SHS continued to be negatively associated with nonverbal reasoning skills after adjustment for maternal education, maternal smoking during pregnancy, and maternal reports of exposure to SHS during pregnancy in separate models.

Conclusions: Children who grow up in an environment with adults who smoke are vulnerable to several social and environmental risk factors. The findings of this study suggest that exposure to SHS during early childhood should also be considered as a potential variable in the risk trajectory and as a marker of other associated risks when formulating public health intervention and prevention strategies.

Keywords: Secondhand smoke, cognition, preschoolers, nicotine, nonverbal reasoning ability

Introduction

There is substantial evidence to support the assertion that maternal smoking during pregnancy is associated with health risks such as preterm delivery, low birth weight, behavioral problems, psychiatric disorders, and neurocognitive impairments in children (1,2). Despite this, the prevalence of smoking during pregnancy in the United States alone has been estimated to occur among 13.5% of pregnant women (3). More recent research into tobacco use has focused on exposure to secondhand smoke (SHS) and passive smoking postnatally and its negative consequences on child development (4). SHS is smoke that is emitted from burning tobacco products (e.g., cigarettes, cigars) or smoke that has been exhaled or breathed out by a person who is smoking. There is no known safe level of SHS; therefore, any exposure to SHS is of concern (5). Approximately 60% of children between the ages of 4 and 11 years are exposed to SHS in the United States (6), with a high proportion of exposure happening in the home or in a car (7). The Centers for Disease Control and Prevention reports that 43.8 million adults in the United States are currently smokers, with men reporting higher rates of smoking (21.6%) as compared with women (16.5%) (3). The elevated levels of smoking among the general population have become an adverse environmental risk factor that can affect the children of non-smoking women.

Similar to the risks associated with maternal smoking during pregnancy, children who are
exposed to SHS during the prenatal period also face adverse health risks, such as neurodevelopmental problems and cognitive impairment (8,9). Prenatal exposure to tobacco smoke has been found to be associated with psychiatric disorders such as attention-deficit/hyperactivity disorder (ADHD) (10,11), conduct disorder (CD), and oppositional defiant disorder (ODD) (12). In a review of the literature, Linnet and colleagues (13) posited a strong association between exposure to tobacco smoke during pregnancy, diagnostic ADHD, and ADHD symptoms in children. They also reported psychological stress during pregnancy to exert a modest contribution to ADHD symptoms in children. It has been reported that mothers who smoke during pregnancy often continue to smoke after childbirth (14,15), which suggests that children with ADHD and externalizing behavior problems are at risk for prenatal environmental exposure as well as postnatal SHS. Despite the evidence showing cognitive and academic deficits among young children with ADHD (16,17) and externalizing disorders (18,19), the effect of postnatal SHS exposure on child development—especially in the area of cognitive development—has not been extensively explored. Children and adolescents between the ages of 5 and 17 years with postnatal tobacco smoke exposure have been found to exhibit cognitive deficits and difficulties with academic functioning (20-23). Bauman and colleagues (20) found household exposure to SHS to be negatively associated with achievement test scores, language, and spelling scores among children in eighth grade. Eskenazi and Trupin (24) reported lower neurobehavioral assessment scores (after controlling for covariates, including SHS exposure in utero) at the age of 5 years among children whose mothers smoked 20 or more cigarettes a day. Results from a longitudinal study by Breslau and colleagues (21) that compared children of smoking mothers with those of non-smoking mothers also found SHS exposure at the age of 5 years to be associated with reductions in intelligence tests scores at the ages of 6, 11 and 17 years. However, this association was no longer statistically significant after accounting for maternal intelligence and education.

Few studies have explored the association between cognitive functioning and postnatal SHS exposure among preschool-aged children, but this is a developmental period that may be of unique importance due to rapid brain changes and possible sensitive periods in brain development. A recent study of preschool-aged children by Jedrychowski and colleagues (8) failed to find an association between postnatal environmental tobacco smoke exposure (as measured by the number of cigarettes smoked at home daily in the presence of the child) and the Mental Development Index of the Bayley Scales of Infant Development at the ages of 12, 24 or 36 months. Similar negative findings were reported by Julvez and colleagues (25), who found that the mother’s postnatal smoking level was not negatively associated with any of the subtests of the McCarthy Scales of Children’s Abilities in a cohort of 4-year-old Spanish children. A study by Baghurst and colleagues (26) found significantly lower scores on the Mental Development Index of the Bayley Scales of Infant Development at the age of 2 years and on the subtests on the McCarthy Scales of Children’s Abilities at the age of 4 years in a sample of Australian children with postnatal exposure to the mother’s smoking. However, these scores were attenuated after accounting for socioeconomic status, quality of the home environment, and mother’s intelligence.

The measure of postnatal smoking exposure in the preceding studies relied primarily on interviews with the mother and did not include any biomarker confirmation, which is the most valid measure of exposure (27,28). In addition, the cognitive measures used in the studies of preschool-aged children are limited to more general measures of cognitive performance, such as the Bayley Scales of Infant Development and the McCarthy Scales of Children’s Abilities. To date, no published study has explored the effect of SHS exposure on the development of specific higher-order cognitive abilities, such as reasoning and problem solving. Children’s reasoning and problem-solving skills have been found to be strongly correlated with general intelligence (29) and working memory (30,31), which are known to be good predictors of academic ability (32-35). Language skills develop rapidly during the preschool years. Thus, nonverbal reasoning abilities are considered to be reliable indices of cognitive development in young children, because limited language skills make performance on the verbal scales of standard intelligence tests somewhat challenging.

More importantly, the roles of smoking-associated neurobehavioral outcomes (e.g., ADHD, CD, ODD) have not been well investigated when studying the relationship between postnatal SHS exposure and cognitive abilities in preschool-aged children. Preschool-aged children are a vulnerable population at a higher risk for SHS exposure because they may spend a large amount of time in the home or in the physical proximity of a caregiver who might be smoking in their presence (36). In addition, the preschool period is a time of rapid brain development, with potential sensitive periods during which the brain may be more affected by environmental exposures (37). Related to this idea is
that the identification of cognitive difficulties during the preschool years is important for early intervention strategies that may help to mitigate negative consequences. Thus, a better understanding of SHS exposure and its effects on cognition—particularly in younger preschool-aged children—is of great importance.

The current analysis attempts to address some of the existing limitations and to extend the literature by using a community-based sample (oversampled for psychopathology) of preschool children between the ages of 4 and 6 years to explore the effects of SHS exposure (using saliva cotinine values) on nonverbal reasoning abilities. The main goals of this study are as follows:

1) To examine if exposure to SHS is associated with deficits in nonverbal reasoning among preschool-aged children (after accounting for selected potential covariates that influence cognitive development); and

2) To examine whether the association between SHS and nonverbal reasoning among preschool-aged children is mediated by another smoking-associated neurobehavioral outcome, specifically ADHD, CD, or ODD.

Methods
Sample
Children between the ages of 3.0 and 5.11 years were recruited from community daycare, preschool, and primary care sites in the St. Louis area for a longitudinal study focused on early childhood depression: The Preschool Depression Study. These sites were selected at random with the use of a geographically stratified method (38). Children were oversampled for depressive disorders on the basis of parent responses to a validated screening checklist: The Preschool Feelings Checklist (39). A group of children with disruptive symptoms and a smaller group of healthy children were also recruited as psychiatric and healthy controls, respectively. Preschoolers with chronic medical or neurological problems, mental retardation, or autistic spectrum disorders were excluded. The study was approved by the Institutional Review Board at Washington University School of Medicine in St. Louis. Caregivers provided written informed consent, and children provided verbal assent when this was appropriate for their age. This longitudinal study is ongoing, and the data reported in the current article are from the second annual wave of data collection. As a part of an add-on study to examine the effects of SHS exposure on behavioral outcomes (K12 DA 000357; Principal investigator: Tandon), cotinine was assayed from 70 saliva samples that were originally obtained in the laboratory during the second and third annual waves of the study for another purpose. The current analysis included only the children with valid measures of salivary cotinine at the ages of 4 and 6 years, which resulted in 54 participants. Cotinine measures were not available when the quantity of saliva was insufficient to complete testing. For detailed information about this cotinine methodology, see the description later in this article as well as the research by Tandon and colleagues (40).

Exposure to Secondhand Smoke
Exposure to SHS was estimated by levels of salivary cotinine, which is a reliable biomarker of nicotine exposure (27). Saliva samples were collected and frozen during the second and third annual assessment waves (November 2004 through June 2006 and October 2005 through April 2007, respectively), when the average ages of the children were 4 and 6 years, respectively. Additional information related to maternal smoking during pregnancy and after pregnancy as well as maternal recall of the child’s exposure to SHS at the ages of 4 and 6 years was obtained via telephone interview at a later stage, when the average age of the child was 12.1 years (standard deviation, 8 months). All questions were adapted from the Timeline Followback interview method (41).

Maternal recall of smoking during pregnancy was established with the use of the following questions:

- How much/often did you smoke in your first trimester?
- What was the least you smoked during your first trimester?
- What was the most you smoked during your first trimester?

The same questions were repeated for the second and third trimesters. Similar questions were used to establish maternal recall of SHS exposure during pregnancy and after birth. Maternal recall of SHS during pregnancy was determined by the following questions:

- Thinking back during your pregnancy, how many hours per day were you in the same room with someone smoking cigarettes during your first trimester typically?
- How many hours per day were you in the same room with someone smoking cigarettes during your first trimester at the least?
- How many hours per day were you in the same room with someone smoking cigarettes during your first trimester at the most?

The same questions were repeated for the second and third trimesters.
Maternal recall of SHS exposure after birth was determined by the following questions:

- Can you recall, if any, how many hours per day your child was exposed to cigarette smoke at age 4 typically?
- Can you recall, if any, how many hours per day your child was exposed to cigarette smoke at age 4 at the least?
- Can you recall, if any, how many hours per day your child was exposed to cigarette smoke at age 4 at the most?

The same questions were repeated to assess exposure at the age of 6 years. Additional questions related to smoking were also considered, such as the following:

- Do you currently smoke?
- Have you smoked since your child was 6 months old (even just 1 cigarette)?
- How many hours per day is your child in the same room with someone who is smoking cigarettes typically/at the least/at the most?

Fifty children had a measurable level of cotinine at the age of 4 years, 45 children had a measurable level at the age of 6 years, and 39 children had measurable levels at the ages of both 4 and 6 years. For children who had cotinine measures at both time points, the highest level of cotinine was used for the analysis. Because the nonverbal reasoning measure used in the current analysis was administered during the second wave, when the children were between 4 and 6 years old, responses to the preceding smoking-related questions from the retrospective maternal interview were supplemented to determine SHS exposure before that period.

**Cognitive Measures: Nonverbal Reasoning Ability**

Children were individually tested with a range of cognitive tests. For the current study, we focused on two of these tests: the pattern construction and picture similarities subtests from the nonverbal reasoning component of the Differential Ability Scale (42). The nonverbal reasoning tests of the Differential Ability Scale have been found to display good convergent validity with other established measures of nonverbal reasoning, such as the performance intelligence component of the Wechsler Scales of Intelligence for Children (42-44).

**The Pattern Construction Subtest**

The pattern construction subtest is a part of the preschool level assessments in the cognitive battery of the Differential Ability Scale, and it has been established as a reliable measure of nonverbal reasoning ability among preschool-aged children (42). The subtest required the children to construct a design. For each trial, the child was shown a pattern made with flat squares or solid cubes with black and yellow patterns on each side, and he or she was then asked to reconstruct the pattern. Standardized scoring and recording procedures were used.

**The Picture Similarities Subtest**

This picture similarities subtest is also a part of the preschool level assessments of the cognitive battery of the Differential Ability Scale, and it has been found to be a reliable measure of preschool-aged children’s nonverbal reasoning ability (42). For each trial of this test, the children were shown a row of four pictures and then given a card with a fifth picture. Each child was required to place the fifth card under one of the first four pictures that shared a common element or concept (42). Standard administration procedures were followed.

**Attention-Deficit/Hyperactivity Disorder, Conduct Disorder, and Oppositional Defiant Disorder**

The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) ADHD, CD, and ODD diagnoses were based on parent reports on the Preschool Age Psychiatric Assessment (45). This assessment has been established as an age-appropriate, comprehensive, diagnostic interview for the assessment of preschoolers with good test-retest reliability (κ = 0.74) (46). The final diagnoses were derived with the use of computerized DSM-IV–based algorithms, which are standard for this measure. In the subsample included in these analyses, only 7.4% of participants (N = 4) qualified for a DSM-IV diagnosis of ADHD, whereas 5.6% (N = 3) and 13.0% (N = 7) qualified for DSM-IV diagnoses of CD and ODD, respectively. Thus, for the current analysis, a dimensional severity score was created by summing the number of ADHD, CD, and ODD symptoms. This estimate of ADHD and externalizing severity had possible values that ranged from 0 to 36.

**Covariates**

Sociodemographic covariates included sex, age, and an income-to-needs ratio. The income-to-needs ratio was defined as the total family income divided by the federal poverty level based on family size for the year most proximal to data collection. This ratio was calculated with the use of baseline data from the Preschool Depression Study. Caregivers’ responses related to family income and total number of individuals living in the household were
included in the calculation (47). Maternal education level, maternal prenatal smoking, and prenatal exposure to SHS were also used as covariates in supplementary analyses.

**Statistical Analysis**
The relationship between exposure to SHS and nonverbal reasoning abilities was explored with the use of linear regression and mediation analyses. All statistical analyses were performed using SAS software (version 9.3). The age and sex of the child as well as the income-to-needs ratio were considered as potential covariates in all analyses. A hierarchical regression model was conducted with sociodemographic variables (i.e., age, sex, and income-to-needs ratio) entered in step 1; ADHD, CD, and ODD symptoms entered in step 2; and cotinine measures entered in step 3 to estimate the unique and shared contribution of each variable for predicting nonverbal reasoning abilities. A mediation model was tested using the Process procedure for SAS by calculating bias-corrected 95% confidence intervals using bootstrapping with 10,000 resamples (48,49). This model was used to determine if the relationship between exposure to SHS and nonverbal reasoning was mediated by ADHD and the severity of externalizing disorder symptoms.

The two measures of nonverbal reasoning ability (i.e., the pattern construction and picture similarities subtests of the Differential Ability Scale) showed a significant correlation \( r = 0.545, p < .01 \), so an average of the \( z \)-scores of the two subtest values was calculated for further analysis. The skew and kurtosis values for all of the variables considered met the criteria for normality (50), except for the skewness index for the measure of SHS exposure. Because the skewness index for the cotinine levels was more than 1.00, a logarithmic transformation was used to normalize the distribution. Winsorising was used to account for an outlier with a cotinine measure that was more than three standard deviations above the mean.

**Results**

**Sample Characteristics**
Sociodemographic information about the population sample is presented in Table 1. All children were between the ages of 4.72 and 6.11 years (mean age, 5.51 years; standard deviation, 0.32 years). Nineteen percent of the children were from low-income families with annual family incomes of less than $20,000. Only 7.4% of the mothers reported an education level of a high-school diploma or lower; 35.2% reported completing some college, whereas a majority (57.4%) reported completing 4-year degrees or receiving graduate education or above. Ten mothers reported that they were current smokers at the time of the retrospective interview.

**TABLE 1. Demographic Characteristics of 54 Children Between the Ages of 4 and 6 Years With Cotinine Measures***

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school diploma</td>
<td>7.4</td>
<td>4</td>
</tr>
<tr>
<td>Some college</td>
<td>35.2</td>
<td>19</td>
</tr>
<tr>
<td>4-year college degree</td>
<td>27.8</td>
<td>15</td>
</tr>
<tr>
<td>Graduate education</td>
<td>29.6</td>
<td>16</td>
</tr>
<tr>
<td>Child DSM IV, ADHD</td>
<td>7.4</td>
<td>4</td>
</tr>
<tr>
<td>Child DSM IV, CD</td>
<td>5.6</td>
<td>3</td>
</tr>
<tr>
<td>Child DSM IV, ODD</td>
<td>13.0</td>
<td>7</td>
</tr>
<tr>
<td>Maternal age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>5.51</td>
<td>0.32</td>
</tr>
<tr>
<td>Child ADHD and externalizing symptoms (range, 0 to 21)</td>
<td>5.17</td>
<td>4.87</td>
</tr>
<tr>
<td>Income-to-need ratio (range, 0 to 4.74)</td>
<td>2.32</td>
<td>1.36</td>
</tr>
</tbody>
</table>

*There were 54 children with cotinine levels at age 4, age 6, or both age 4 and age 6. There were 50 children with cotinine levels at age 4 and 45 children with cotinine levels at age 6.

**Correlational Analyses**
Descriptive statistics and the intercorrelations among the child’s age and sex, the maternal education level, the income-to-needs ratio, the ADHD and externalizing disorder symptoms, the cotinine levels, and the nonverbal reasoning skills are presented in Table 2. The child’s age, the maternal education level, and the income-to-needs ratio were positively correlated with children’s nonverbal reasoning abilities \( r = 0.363, p < .01; r = 0.355, p < .01; r = 0.429, p < .01 \), respectively. The log cotinine value was negatively correlated with maternal education \( r = -0.537, p < .001 \), nonverbal reasoning ability \( r = -0.471, p < .001 \), and income-to-needs ratio \( r = -0.571, p < .001 \). The log cotinine value continued to be negatively correlated with nonverbal reasoning after accounting for the child’s age and sex, the income-to-needs ratio, and the ADHD and externalizing disorder symptoms \( r = -0.285, p = .045 \). The relationship between the log cotinine value and nonverbal reasoning is shown in Figure 1.
TABLE 2. Descriptive Statistics and the Intercorrelations Among Nonverbal Reasoning, Cotinine Measures, and Sociodemographic Variables

<table>
<thead>
<tr>
<th>Measures</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Gender</td>
<td>-0.030</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Maternal education</td>
<td>-0.051</td>
<td>-0.337*</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Income-to-need-ratio</td>
<td>0.181</td>
<td>-0.347*</td>
<td>0.708***</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. ADHD, CD, and ODD symptoms</td>
<td>-0.001</td>
<td>-0.084</td>
<td>-0.073</td>
<td>-0.111</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>6. Nonverbal reasoning</td>
<td>0.363**</td>
<td>0.003</td>
<td>0.355**</td>
<td>0.429**</td>
<td>0.092</td>
<td>-</td>
</tr>
<tr>
<td>7. Contine (log)</td>
<td>-0.304*</td>
<td>0.119</td>
<td>0.537***</td>
<td>0.571***</td>
<td>0.239</td>
<td>-0.471**</td>
</tr>
</tbody>
</table>

Descriptive Statistics

<table>
<thead>
<tr>
<th>Measures</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern construction subtest (raw score)</td>
<td>21.24</td>
<td>6.72</td>
</tr>
<tr>
<td>Picture similarities subtest (raw score)</td>
<td>15.31</td>
<td>3.53</td>
</tr>
<tr>
<td>Cotinine level</td>
<td>1.35</td>
<td>2.38</td>
</tr>
</tbody>
</table>

*Correlations significant at p < .05; **Correlations significant at p < .01; ***Correlations significant at p < .001

Note. ADHD=attention-deficit/hyperactivity disorder; CD=conduct disorder; ODD=oppositional defiant disorder

FIGURE 1. The negative relationship between log cotinine and nonverbal reasoning

Regression Analysis

Results from the hierarchical regression model are presented in Table 3. Overall, sociodemographic variables (i.e., age, sex, and income-to-needs ratio) accounted for nearly 30% of the variance in the children’s nonverbal reasoning. Adding ADHD, CD, and ODD symptoms to the model in step 2 did not significantly improve the model (change $F_{1,49} = 1.74, p = .194$). The log cotinine values continued to account for a small but significant (6%) proportion of the variance when added to the model in step 3, after accounting for sociodemographic variables and ADHD and externalizing disorder symptoms (change $F_{1,48} = 4.24, p = .045$).
Secondhand smoke and nonverbal reasoning

### TABLE 3. Hierarchical Regression Model Testing the Effects of Secondhand Smoke Exposure on Nonverbal Reasoning in 54 Children Between the Ages of 4 and 6 Years

<table>
<thead>
<tr>
<th>Model</th>
<th>R²</th>
<th>Estimate</th>
<th>SE</th>
<th>T Value</th>
<th>p Value</th>
<th>Effect Size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>0.291</td>
<td></td>
<td></td>
<td>F = 6.83</td>
<td>&lt;.001</td>
<td>0.10</td>
</tr>
<tr>
<td>Age</td>
<td>0.66</td>
<td>0.28</td>
<td>2.39</td>
<td>.021</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>0.24</td>
<td>0.19</td>
<td>1.27</td>
<td>.210</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Income-to-needs ratio</td>
<td>0.23</td>
<td>0.07</td>
<td>3.35</td>
<td>.002</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>0.315</td>
<td></td>
<td></td>
<td>F = 5.64</td>
<td>&lt;.001</td>
<td>0.20</td>
</tr>
<tr>
<td>Age</td>
<td>0.65</td>
<td>0.27</td>
<td>2.38</td>
<td>.022</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>0.27</td>
<td>0.19</td>
<td>1.44</td>
<td>.156</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Income-to-needs ratio</td>
<td>0.25</td>
<td>0.07</td>
<td>3.53</td>
<td>&lt;.001</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>ADHD, CD and ODD symptoms</td>
<td>0.02</td>
<td>0.02</td>
<td>1.32</td>
<td>.194</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td>0.371</td>
<td></td>
<td></td>
<td>F = 5.65</td>
<td>&lt;.001</td>
<td>0.20</td>
</tr>
<tr>
<td>Age</td>
<td>0.51</td>
<td>0.28</td>
<td>1.84</td>
<td>.072</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>0.24</td>
<td>0.18</td>
<td>1.34</td>
<td>.186</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Income-to-needs ratio</td>
<td>0.16</td>
<td>0.08</td>
<td>1.99</td>
<td>.053</td>
<td>0.20</td>
<td></td>
</tr>
<tr>
<td>ADHD, CD and ODD symptoms</td>
<td>0.03</td>
<td>0.02</td>
<td>1.78</td>
<td>.082</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Log cotinine</td>
<td>-0.34</td>
<td>0.17</td>
<td>-2.06</td>
<td>.045</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

*Measured by partial eta-squared

Note. ADHD=attention-deficit/hyperactivity disorder; CD=conduct disorder; ODD=oppositional defiant disorder

### FIGURE 2. Model illustrating the relationship between log cotinine levels and nonverbal reasoning in 54 children between the ages of 4 and 6 years. The dotted arrow indicates a significant direct effect of log cotinine on nonverbal reasoning. The solid arrows indicate total effects, which were not significant. Attention-deficit/hyperactivity disorder, conduct disorder, and oppositional defiant disorder symptoms did not mediate the relationship between log cotinine values and nonverbal reasoning.

The negative relationship between log cotinine levels and nonverbal reasoning skills persisted after accounting for prenatal smoking ($t = -2.06$, $p = 0.045$), and prenatal exposure to SHS ($t = -2.19$, $p = .034$) as additional sociodemographic covariates. Nonverbal reasoning and log cotinine values continued to be marginally negatively associated after accounting for maternal education (in lieu of income-to-needs ratios) ($t = -1.95$, $p = .058$). This negative relationship was not present when both maternal education and income-to-needs ratios were included in the model. Maternal education and income-to-needs ratios showed a strong correlation ($r = 0.708$, $p < .001$), so both variables were not included in the model.

### Mediation Models

Figure 2 shows a mediation design that investigates whether the effect of SHS exposure on nonverbal reasoning is indirectly influenced by ADHD and...
externalizing disorder symptoms. In keeping with the prior analyses, children’s age and sex and the income-to-needs ratio were included as covariates. The direct effect of SHS on nonverbal reasoning was −0.34 (standard error, 0.17; p = .045; 95% confidence interval, −0.67 to −0.01), which indicates that exposure to SHS is negatively associated with children’s nonverbal reasoning. The indirect effect of SHS exposure on nonverbal reasoning through ADHD and externalizing disorder symptoms was 0.06 (bootstrap standard error, 0.07; 95% bootstrap confidence interval, −0.03 to 0.26), which demonstrates that ADHD and externalizing disorder symptoms did not mediate the relationship between SHS and nonverbal reasoning in this sample.

Discussion

The current study assessed the strength of the relationship between exposure to SHS, associated psychopathology (i.e., ADHD, CD, and ODD symptoms), and nonverbal reasoning skills among preschool children between the ages of 4 and 6 years. The results indicated that exposure to SHS is negatively associated with nonverbal reasoning skills in preschool-aged children even after accounting for selected sociodemographic variables and associated psychopathology. If children have adults in their lives who smoke in their presence, this is an indication that these children are exposed to several social and environmental risk factors that can have adverse effects on their development. The results of the current study highlight the importance of considering exposure to SHS during early childhood as a potential variable in the risk trajectory and as a marker of other associated risks that should be taken into account when formulating intervention and prevention strategies.

These findings are to some extent consistent with previous work by Baghurst and colleagues (26), who also reported significantly lower cognitive performance in a group of children with SHS exposure between the ages of 2 and 4 years in a longitudinal study. However, those researchers reported that this adverse relationship was no longer significant after accounting for socioeconomic status, the quality of the home environment, and the mother’s intelligence. This highlights the possibility that this association can be accounted for by varied social and environmental factors that influence the child-rearing environment but that were not considered in the current study. Similarly, Julvez and colleagues (25) and Jedrychowski and colleagues (8) did not find postnatal SHS exposure to be associated with an elevated risk for delays in cognitive development. None of these three studies used biomarker information to assess exposure to SHS, measured reasoning skills, or incorporated the effects of smoking-related childhood psychopathology on cognitive development.

To our knowledge, the current study is the first to use biomarker information—in this case, salivary cotinine levels—when studying the relationship between SHS and cognitive abilities in preschool-aged children. The use of the biomarker overcomes some of the limitations in the extant literature related to the use of retrospective maternal reports. The results of the current study are consistent with the studies by Cho and colleagues (22) and Yolton and colleagues (23), both of which used biomarker information (serum or urine cotinine) to assess exposure to SHS in older children. Yolton and colleagues (23) reported high serum cotinine levels to be associated with reduced math scores, reading scores, working memory, and spatial reasoning in a large sample of children between the ages of 6 and 16 years from the third wave of the National Health and Nutrition Examination Survey. However, these negative relationships—except for the reading scores—were attenuated after accounting for prenatal smoking exposure. In the current study, further analyses indicated that cotinine measures and nonverbal reasoning were negatively associated even after accounting for maternal prenatal smoking and SHS exposure during the prenatal period. However, a limitation of our design was that maternal prenatal smoking and SHS exposure during pregnancy were based on retrospective maternal self-reports.

Similarly, Cho and colleagues (22) reported higher urine cotinine levels to be associated with a range of cognitive deficits, including lower word-reading scores and overall slower performance in a sample of Korean children between the ages of 8 and 11 years. Aside from the studies that included biomarker information, several studies that involved the use of maternal reports have shown elevated SHS exposure to be negatively associated with academic abilities (20,51) and intelligence quotient scores (21) in older children. These findings suggest that, although prenatal smoking exposure has adverse effects on children’s cognitive development at younger ages, the postnatal environment and SHS exposure also seem to exert a significant negative influence on children’s cognitive development as they get older (4). Therefore, studies that investigate postnatal SHS exposure can add important information to understanding risk trajectories (as compared with those studies that focus exclusively on prenatal exposure).

The current study is also the first that we are aware of that includes a comprehensive and state-of-the-art assessment of early childhood
Secondhand smoke and nonverbal reasoning

psychopathology and that therefore can meaningfully account for the influence of comorbid psychopathology on cognitive skills in the context of SHS exposure in a group of preschool children. Children with ADHD are known to show deficits in a range of cognitive tasks, including inhibitory control, working memory, long-term memory, and reasoning abilities (52-54). ADHD is also known to be a risk factor for cigarette smoking (55). Prenatal tobacco smoking has been found to be associated with both inattentive and hyperactive/impulsive symptoms in offspring (10,11), and greater exposure to SHS has also been found to be associated with more severe ADHD symptoms among preschool children (40). Similarly, studies have shown prenatal smoking and exposure to SHS to be associated with CD-related and ODD-related symptoms in children (56,57). In addition, children with externalizing disorders have been found to have lower intelligence levels, academic difficulties, and deficits in the areas of executive functioning (19,58,59). Therefore, accounting for childhood ADHD and externalizing disorder symptoms as possible mediators in the relationship between SHS exposure is of importance given that children with these characteristics may be in a position to bear the risks of prenatal and postnatal exposure to tobacco smoke.

Results in the current study suggest that poor performance in nonverbal reasoning was not mediated by the presence of ADHD and externalizing disorder symptoms. Nonverbal reasoning is strongly correlated with intelligence levels (29) and working memory (30,31), which are known to be predictive of academic abilities such as mathematical reasoning and reading comprehension (33,34). This indicates the importance of considering the long-term effects of SHS exposure on preschoolers’ cognitive deficits when planning early interventions. It also suggests that public health programs should consider the deleterious effects of SHS exposure during early childhood on cognitive outcomes.

Some limitations of this study are noteworthy. First of all, the current study has a relatively small sample size. Considering the unique population that is being studied (i.e., preschool-aged children), it is of note that we were able to detect an effect even in a small sample of 54 children. One of the major limitations is that we are unable to disentangle the effects of prenatal and postnatal exposure to SHS. Postnatal exposure was measured with the use of saliva cotinine values, and prenatal exposure was based on the maternal interview. Eight mothers (15%) reported that they smoked during pregnancy, and 28% reported that they were exposed to SHS during the first, second, or third trimester. Thus, some of the children in the sample were at risk for both prenatal and postnatal smoking exposure, which makes it difficult to disentangle the role of each on cognitive performance. It should also be noted that maternal reports may be limited by retrospective recall bias, because the smoking interview was conducted during a later stage of the study.

It has also been reported that women who smoke during pregnancy or during the child-bearing and child-rearing years are more likely to live in poverty, to be less educated, and to abuse other substances (e.g., alcohol); they also often suffer from anxiety and depression (2). Children who live in poverty are at a higher risk of being exposed to other environmental hazards (e.g., lead, certain chemicals) (8). All of these factors, in addition to SHS exposure, can have adverse effects on a child’s cognitive development. It is also possible that other unmeasured maternal characteristics (e.g., maternal intelligence, parenting style) could influence these results. Although the income-to-needs ratio was considered a covariate because it can be considered a proxy for socioeconomic status, we were unable to identify and control for many key social and environmental factors that may have influenced the findings of this study. We also used symptom counts rather than formal diagnostic criteria to define ADHD, ODD, or CD because of the limited number of children who met the criteria for a formal DSM-IV diagnosis. This might have reflected a milder risk and possibly attenuated the strength of the relationship between ADHD, externalizing disorders, SHS exposure, and cognitive performance. Finally, because this is a cross-sectional study, we cannot make any causal inferences about the nature of the relationship between SHS exposure and cognitive performance.

Despite these limitations, to our knowledge, this is the first study to use a biomarker (saliva cotinine) to measure SHS exposure. It is also the first study to consider an age-appropriate comprehensive assessment of related psychopathology as a potential mediating variable that could influence cognitive performance among preschool-aged children. Overall, the findings obtained by this study may be helpful to clinical practice and public policy by creating an awareness of the long-term negative effects of passive smoking, and they may be useful when formulating early intervention strategies to help high-risk child populations. Accounting for the comorbidity of ADHD and externalizing disorders in mothers and children also might be of importance when tailoring prevention, intervention, and treatment protocols. Future studies to investigate these risk relationships in larger samples are indicated. Large epidemiological samples that
control for maternal smoking during pregnancy would further help to disentangle some of the confounding effects of the present study. Ideally, larger prospective studies that include only participants exposed to postnatal (not prenatal) SHS would help to further inform the separate effects of these exposures on various neurocognitive domains. In addition, parental characteristics—especially maternal intelligence—should be considered as one of the key variables that influence this relationship. Controlling for the many key covariates associated with SHS exposure will continue to be a challenge in related investigations. Longitudinal studies will be of particular importance to determine if the cognitive deficits identified persist with age and intervention. However, it should be noted that results like those of the present study are important because they can help to define the potential likely and unlikely causal variables and direct the focus of longitudinal studies, which are inherently much more effortful and expensive.

Clinical Significance
Findings indicate that exposure to SHS is one of the numerous social and environmental risk factors that influences early childhood cognitive outcomes. These findings highlight the importance of considering the long-term effects of SHS exposure along with other potential risk factors when planning early interventions.

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References

124
Secondhand smoke and nonverbal reasoning


