Is exposure to secondhand smoke associated with cognitive parameters of children and adolescents?—a systematic literature review*

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\textbf{A B S T R A C T}

\textbf{Purpose:} Despite the known association of second hand smoke (SHS) with increased risk of ill health and mortality, the effects of SHS exposure on cognitive functioning in children and adolescents are unclear. Through a critical review of the literature we sought to determine whether a relationship exists between these variables.

\textbf{Methods:} The authors systematically reviewed articles (dated 1989–2012) that investigated the association between SHS exposure (including in utero due to SHS exposure by pregnant women) and performance on neurocognitive and academic tests. Eligible studies were identified from searches of Web of Knowledge, MEDLINE, Science Direct, Google Scholar, CINAHL, EMBASE, Zetoc, and Clinicaltrials.gov.

\textbf{Results:} Fifteen articles were identified, of which 12 showed inverse relationships between SHS and cognitive parameters. Prenatal SHS exposure was inversely associated with neurodevelopmental outcomes in young children, whereas postnatal SHS exposure was associated with poor academic achievement and neurocognitive performance in older children and adolescents. Furthermore, SHS exposure was associated with an increased risk of neurodevelopmental delay.

\textbf{Conclusions:} Recommendations should be made to the public to avoid sources of SHS and future research should investigate interactions between SHS exposure and other risk factors for delayed neurodevelopment and poor cognitive performance.

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\textbf{Introduction}

Exposure to tobacco smoke is harmful and is associated with ill health and mortality [1]. A relationship has been well established between active smoking and an increased risk of cognitive decline and dementia [2,3]. However, the relationship between exposure to passive smoking (i.e., secondhand smoke [SHS]) and cognitive functioning remains controversial. Several studies have been conducted over the last two decades to investigate the association with cognitive parameters, with conflicting findings [4–8]. In 1999, a systematic literature review [9] was published to examine the relationship between SHS exposure and cognitive functioning in children with no solid conclusion. Two later articles looked at the impact of SHS exposure on childhood outcomes, but they mostly focussed on maternal smoking in pregnancy and did not comprehensively review the literature regarding other forms of exposure [10,11]. Since the 1999 review [9], a substantial number of studies have been published to investigate the effect of SHS on cognition parameters. At present, approximately 30% of the world’s population is exposed to SHS [12], particularly in children [13], making the implications of exposure a potentially major health care challenge. The aim of the present review was, therefore, to build on the existing literature to provide a systematic evaluation of the current literature in this field to determine whether or not exposure to SHS is associated with cognitive parameters in children and adolescents.

\textbf{Methods}

We searched Web of Knowledge, MEDLINE, Science Direct, Google Scholar, CINAHL, EMBASE, Zetoc, and Clinicaltrials.gov (date 2013–2012).
range unrestricted) to identify articles eligible for inclusion in this review. We used combinations of keywords for SHS (tobacco, tobacco smoke, environmental tobacco smoke, passive smoking, and secondhand smoke) and cognitive functioning (cognition, cognitive function, cognitive impairment, dementia, executive function, and memory). Abstracts were retrieved and screened and full texts of all articles relating to the association between SHS exposure and cognitive functioning were retrieved for further evaluation. We also manually searched the bibliographies of selected articles for additional studies (see Fig. 1 for schematic presentation of identifying articles for review). The literature search was completed in February 2012.

To be eligible for inclusion in this review, an article must report data from an observation study that included both a measure of exposure to SHS (pre- or postnatal) and at least one objective measure of cognitive functioning or impairment using any summary measure. Retrieved articles were excluded if they did not clearly define the exposure and outcome variables or if the association of cognitive performance with SHS exposure could not be determined independently of other toxins such as other urban pollutants or illicit drug exposure in utero due to these factors being combined into one variable. Articles were also excluded if no statistical evidence relevant to our research question was presented (e.g., data not shown) or were not original research articles. As the impact of maternal smoking in pregnancy on cognitive outcomes has been reviewed in detail elsewhere [14], the aim of the present article was to focus on SHS not due to maternal smoking. Articles that had data only on maternal smoking in pregnancy were therefore excluded in the present review. We focused on studies of children (age ≤ 18 years) to examine the associations of SHS with cognitive parameters as their cognitive function was in development and sensitive to SHS. We therefore excluded articles involving older adults (n = 1) [15].

Risk of bias was assessed qualitatively for each study and any issues arising are discussed below for each article individually. For all articles, the following data were extracted independently by three reviewers (A.C., R.C., L.L.): year of publication, the study design, sampling of participants, country, the number of participants, mean participant age, participant gender, the percentage of participants exposed to SHS, the measurement of SHS, the measurement of cognitive functioning, the covariates included in the analyses, and the outcome of the study.

**Results**

The literature search identified 61 articles, of which 15 met the inclusion criteria and reported sufficient data to be included in the review (Fig. 1). These articles were published between 1989 and 2012, four of which were cross-sectional [16–19] and 11 were prospective [4–8, 20–25]. Two articles presented findings from the U.S.-based Child Health and Development Studies (CHDS) [4, 20]. The age range covered by the studies ranged from 6 months and 17 years. Eleven studies were conducted in the United States, Canada, Europe, or Australia, with the remaining three being carried out in Asia [5, 6, 19]. Five articles used cotinine level as an objective measure of SHS exposure [4, 18, 19, 21, 25], whereas the remainder used questionnaire data from the participant or a parent to estimate exposure. The articles are presented below in three sections: cognitive functioning in children after SHS exposure in utero (n = 7; Table 1), cognitive functioning in preschool children after postnatal SHS exposure (n = 4; Table 2), and cognitive functioning in older children (≥ 5 years) after postnatal SHS exposure (n = 7; Table 3). Where more than one model was presented for results, the results adjusted for the most covariates were included in this review.

**In utero exposure due to mother’s exposure to SHS during pregnancy**

Seven prospective studies investigated the relationship between SHS exposure in utero (due to the mother’s exposure to SHS during pregnancy) and cognitive outcomes. Lee et al. [5] demonstrated a deficit of 2.82 points on the Bayley Scales of Infant Development—Mental Development Index (BSID—MDI) in young infants aged 6 months who had been exposed to tobacco smoke in utero compared with those who were not exposed. This deficit was associated with a 1.36-fold increased risk (95% confidence interval [CI], 1.21 to 4.59) of moderate developmental delay (score ≤ 85).

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**Fig. 1.** Flowchart showing the process of identifying studies for this review.
<table>
<thead>
<tr>
<th>First author (publication year)</th>
<th>Methodology, sample, and location</th>
<th>N</th>
<th>Population/sample characteristics</th>
<th>Measurement of passive smoking in utero</th>
<th>Measures of cognitive functioning</th>
<th>Confounders measured</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eskenazi and Trupin 1995 [4]</td>
<td>Prospective CHDS United States</td>
<td>1310</td>
<td>Mean age 5 y at follow-up 50.5% female 5.3% exposed to SHS</td>
<td>Maternal serum cotinine during pregnancy (exposed/not exposed)</td>
<td>IQ RCPM PPVT</td>
<td>Mother's and father's education, social class, mother's race, child's age, birth order, preschool attendance, and maternal alcohol consumption during pregnancy, family income, mother's race, mother's age, gestational age at first prenatal visit, child's gender, number of parents in the home, and mother's employment status at 5-y follow-up</td>
<td>SHS exposure not associated with unadjusted scores on the RCPM (unexposed: mean = 10.7; 95% CI, 10.6 to 10.9; exposed: mean = 10.5; 95% CI, 10.0 to 11.2) or on the PPVT (unexposed: mean = 52.6; 95% CI, 52.1 to 53.1; exposed: mean = 52.5; 95% CI, 50.7 to 54.4). No change after adjustment.</td>
</tr>
<tr>
<td>Hsieh et al. (2008) [24]</td>
<td>Prospective Taiwan Birth Panel Study (2004–2005) Taiwan</td>
<td>145</td>
<td>Age 2 y % female 89% exposed to SHS</td>
<td>Cord blood cotinine (exposed [cotinine 0.16–14 ng/mL] vs. not exposed [cotinine &lt; 0.16])</td>
<td>Neurodevelopment CDIIT</td>
<td>Maternal education, maternal nationality, family income, infant gender, gestational age, HOME score, postnatal SHS exposure</td>
<td>SHS exposure associated with reduced CDIIT total score ($\beta = -7.89 \pm 2.48, P = .002$), cognitive score ($\beta = -5.4 \pm 2.56, P &lt; .04$), and language score ($\beta = -7.9 \pm 2.44, P = .002$). Significant association between SHS exposure in utero and average neurodevelopment over 3 y ($\beta = -2.17 [-4.01 to -0.34], P = .020$)</td>
</tr>
<tr>
<td>Jedrychowski et al. (2009) [7]</td>
<td>Prospective Participants recruited through two prenatal clinics Poland</td>
<td>457</td>
<td>Assessed at 12, 24, and 36 mo of age 49% female 26.3% exposed to SHS</td>
<td>Interview with mother during second and third trimester of pregnancy (average number of cigarettes smoked daily in the presence of mother during pregnancy)</td>
<td>Neurodevelopment BSID-MDI</td>
<td>Maternal education, parity, breastfeeding, cord blood lead, gender, postnatal SHS exposure. Interaction: blood lead x gender</td>
<td></td>
</tr>
<tr>
<td>Lee et al. (2011) [5]</td>
<td>Prospective Mother's and Children's Environmental Health Study Korea</td>
<td>414</td>
<td>Mean age 6.36 mo 50% female 63.5% exposed to SHS</td>
<td>Interview with mother during pregnancy (exposed vs. not exposed)</td>
<td>Neurodevelopment Normal (&gt;85) vs. delayed (≤85) Bayley Scales of Infant Development second edition Mental Development Index</td>
<td>Residential area, maternal age, prepregnancy BMI, maternal education level, income, infant gender, parity, type of breastfeeding from birth to 6 mo, and birth weight</td>
<td>SHS exposure associated with a 2.82-point decrease in neurodevelopmental score ($\beta = -5.21$ to $-0.44$). SHS exposure associated with an increased risk of moderate mental developmental delay (OR, 2.36; 95% CI, 1.21 to 4.59).</td>
</tr>
<tr>
<td>Makin et al. (1991) [8]</td>
<td>Prospective Ottawa Prenatal Prospective Study Canada</td>
<td>58</td>
<td>Age 6–7 y 52% female 60% exposed to SHS</td>
<td>Interview with mother during pregnancy (exposed/not exposed)</td>
<td>IQ, educational attainment Wechsler Intelligence Scale for Children, Wide Range Achievement Test, Speech and language tests (PPVT, sound blending, Test of Language Development—Primary)</td>
<td>Socioeconomic status</td>
<td></td>
</tr>
<tr>
<td>Perera et al. (2012) [6]</td>
<td>Prospective Recruited from three hospitals China</td>
<td>100</td>
<td>Age 5 y 49% female 70% exposed to SHS</td>
<td>Interview with the mother after delivery (hours per day exposed to SHS)</td>
<td>IQ Wechsler Preschool and Primary Scale of Intelligence</td>
<td>Gestational age, maternal education, cord lead, mother's age, and gender</td>
<td>No significant main effect of hours of SHS exposure on full scale IQ ($\beta = -2.48; 95% CI, -7.00 to 2.04$). Interaction between SHS exposure and exposure to other carcinogenic air pollutants (full-scale IQ: $\beta = -10.10; 95% CI, -18.90 to -1.29$; Verbal IQ: $\beta = -10.35; 95% CI, -19.61 to -1.10$; Performance IQ: $\beta = -7.78; 95% CI, -18.03 to 2.48$)</td>
</tr>
</tbody>
</table>
SHS exposure associated with lower neurodevelopmental scores by 4.6 points (exposed: mean = 82.0, SD = 13.0; unexposed: mean = 86.6, SD = 12.3; P = .007) SHS exposure associated with increased risk of developmental delay and was increased to a 7-point deficit in those whose mothers reported material hardship. No adjustment was made in this study for postnatal SHS exposure, although the following two similar studies did make such an adjustment. Jedrychowski et al. [7] found that BSID–MDI scores at age 3 years were reduced with increasing number of cigarettes smoked in the presence of the mother during pregnancy, with a β-coefficient of −2.17 (95% CI, −4.01 to −0.34). Hsieh et al. [24] showed reduced total (7.9 points), cognitive (5.4 points), and language (7.9 points) scores on the Comprehensive Developmental Inventory for Infants and Toddlers for 2-year-old children whose cord blood contained cotinine levels between 0.16 and 14 ng/mL. The strengths of some of these reductions were modified by specific metabolic gene polymorphisms (CYP1A1 Ile65Val and GSTT1), which appear to affect the toxicity of tobacco smoke.

Two studies investigated the association between SHS exposure in utero and intelligence at age 5 years. Eskenazi and Trupin [4] found no discernible differences in intelligence between those exposed to SHS in utero (indicated by prenatal cotinine levels 2–10 ng/mL) and those without in the CHDS. Adjusted Peabody Picture Vocabulary Test scores were approximately 1 point higher for the exposed group compared with the nonexposed group but this was not significant. Perera et al. [6] demonstrated a deficit of 2.5 points (95% CI, −7.96 to 3.13) in full-scale intelligence scores for each hour of exposure to SHS a day but this did not reach significance (P > .05). However, an interaction was seen with exposure to other air pollutants called polycyclic aromatic hydrocarbons whereby SHS exposure significantly increased the inverse relationship between polycyclic aromatic hydrocarbons and intelligence despite there being no significant main effect of exposure to these toxins.

Makin et al. [8] assessed maternal SHS exposure both inside and outside of the home during pregnancy using maternal self-report. At 6–7 years of age, children who had been exposed to SHS in utero scored approximately 2.8 to 2.9 standard deviation lower on six different measures of intelligence and language (P ≤ .05) compared with those who had not been exposed. In contrast, few discernible differences were seen in scores between groups for assessments of visuospatial abilities and academic achievement.

**SHS exposure and cognition in preschool children**

The association between postnatal SHS exposure and neurodevelopment in very young children was assessed in four prospective studies. Lee et al. [5] showed that the risk of having delayed neurodevelopment was increased by only 6% (P > .05) for exposed compared with nonexposed infants at 6 months. All children had nonsmoking mothers and because it is likely that the greatest source of SHS in this age group would be the mother, exposures in this study may have been too low to see any significant relationships with neurodevelopment. However, other studies measuring maternal smoking have also found no associations with cognition at age 2–4 years. Children recruited to the Port Pirie Cohort Study who were exposed to their mother’s smoking had lower neurodevelopmental scores by approximately 3 points compared with children who were not exposed, but the differences became negligible (approximately 0.5 points) after adjustment for socioeconomic status [22].

Julvez et al. [23] examined data from the Menorca part of the Asthma Multicenter Infants Cohort Study. Children whose
Table 2
Details of studies investigating the relationship between postnatal SHS and cognitive functioning in preschool-aged children

<table>
<thead>
<tr>
<th>First author (publication year)</th>
<th>Methodology and location</th>
<th>N</th>
<th>Population/sample characteristics</th>
<th>Measurement of SHS exposure</th>
<th>Measures of cognitive functioning</th>
<th>Confounders measured</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baghurst et al. (1992) [22]</td>
<td>Prospective Port Pirie Cohort Study Australia</td>
<td>548</td>
<td>Age 2 and 4 y % female (not given) 40% exposed to SHS at age 2 y; 36% exposed to SHS at age 4 y</td>
<td>Interview with mother: exposure to mother’s smoking (exposed/not exposed)</td>
<td>Neurodevelopment: BSID—MDI at age 2 y MSCA—GCI at age 4 y</td>
<td>Socioeconomic status, HOME scores, and maternal IQ (Wechsler Adult Intelligence Scale)</td>
<td>SHS exposure associated with BSID—MDI scores ($\beta = -2.7, P = .04$) and MSCA—GCI scores ($\beta = -3.5, P = .01$). Both scores attenuated after adjustment for the covariates (BSID—MDI: $\beta = -1.76, P = .18$; MSCA—GCI: $\beta = -2.04, P = .52$).</td>
</tr>
<tr>
<td>Jedrychowski et al. (2009) [7]</td>
<td>Prospective Participants recruited through two prenatal clinics Poland</td>
<td>457</td>
<td>Assessed at 12, 24, and 36 mo of age 49% female 19.5% exposed to SHS</td>
<td>Interview with mother: exposure to household SHS (daily number of cigarettes)</td>
<td>Neurodevelopment: (normal vs. delayed development) BSID-MDI</td>
<td>Maternal education, parity, breastfeeding, cord blood lead, gender, and SHS exposure in utero. Interaction: blood lead × gender</td>
<td>SHS exposure not associated with cognitive development at 2 y of age ($\beta = -0.13; 95% CI, -0.834 to 1.092; P = .793$) or 3 y of age ($\beta = -0.38; 95% CI, -0.370 to 1.138; P = .317$).</td>
</tr>
<tr>
<td>Julvez et al. (2007) [23]</td>
<td>Prospective Asthma Multicentre Infants Cohort Study Spain</td>
<td>330</td>
<td>Mean age 4 y % female (not given) 23% exposed to SHS</td>
<td>Interview with mother: exposure to mother’s and father’s smoking (exposed/not exposed)</td>
<td>Neurodevelopment: MCSA: Working memory Memory span Executive function Posterior functions</td>
<td>Home location, maternal alcohol consumption during pregnancy, gender, birth weight and height, breastfeeding duration, school season and age during test administration, examiner, social class, mother’s education, mother’s parity, mother’s marital status, father’s education, maternal smoking during pregnancy</td>
<td>SHS exposure (mother’s smoking postnatal only) not significantly associated with MCSA scores ($\beta = -2.4; 95% CI, -6.3 to 1.4; P = .21$). SHS exposure (father’s smoking) associated with MCSA scores ($\beta = -3.1; 95% CI, -5.9 to -0.3; P = .03$) but attenuated after adjustment for maternal smoking during pregnancy ($\beta = -2.4; 95% CI, -5.4 to 0.6; P = .12$).</td>
</tr>
<tr>
<td>Lee et al. (2011) [5]</td>
<td>Prospective Mother’s and Children’s Environmental Health study Korea</td>
<td>414</td>
<td>Mean age 6.36 mo 50% female 38.5% exposed to SHS</td>
<td>Interview with mother: exposure to household SHS (exposed/not exposed)</td>
<td>Neurodevelopment: Normal (&gt;85) versus delayed (≤85) Bayley Scales of Infant Development second edition Mental Development Index</td>
<td>Residential area, maternal age, prepregnancy BMI, maternal education level, income, infant gender, parity, type of feeding from birth to 6 mo, and birth weight</td>
<td>SHS exposure not associated with increased risk of delayed neurodevelopment (OR, 1.06; 95% CI, 0.54 to 2.08).</td>
</tr>
</tbody>
</table>

BMI — body mass index; MCSA — McCarthy Scales of Children’s Abilities; MSCA—GCI — McCarthy Scales of Children’s Abilities—General Cognitive Index.
<table>
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<tr>
<th>First author (publication year)</th>
<th>Methodology and location</th>
<th>N</th>
<th>Population/sample characteristics</th>
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<th>Confounders measured</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bauman et al. (1989) [16]</td>
<td>Cross-sectional Participants recruited from North Carolina Public Schools United States</td>
<td>973</td>
<td>Age approximately 13 y (eighth graders) 51% female 64% exposed to SHS</td>
<td>Questionnaire completed by mother: exposure to parent or sibling smoking (none, 1 cigarette to 1 pack, 1–2 packs, ≥2 packs)</td>
<td>Academic achievement CAT subtests: Maths Language Reading Spelling Total score</td>
<td>Parent education, age, race, gender, attitude toward smoking, locus of control, friend influence, and sociability. Interactions: Race × Parent Education Gender × Parent Education Race × Age Race × Attitude Toward Smoking Age × Attitude Toward Smoking Locus of Control × Attitude Toward Smoking</td>
<td>SHS exposure associated with lower CAT total score ($\beta = -5.8; P &lt; .018$), language ($\beta = -7.0; P &lt; .008$), and spelling ($\beta = -10.9; P &lt; .001$) scores. Trends between increasing SHS exposure and lower mathematics ($\beta = -4.4; P &lt; .070$) and reading ($\beta = -4.3; P &lt; .093$) scores.</td>
</tr>
<tr>
<td>Bauman et al. (1991) [20]</td>
<td>Prospective CHDS United States</td>
<td>2854</td>
<td>Age 5 y and 9–11 y at follow-up (also used a 15- to 17-y age group but as some were smokers, we excluded them from this review) % female (not given) % exposed (not given)</td>
<td>Interview with mother at each assessment: exposure to parent’s smoking at home (exposed/not exposed; number of cigarettes per day)</td>
<td>IQ Raven Standard Progressive Matrices PPVT</td>
<td>Birth weight, age, gender, mother’s race, mother’s education, father’s education, father’s occupation, family income, mother’s cognitive performance (PPVT), exposure to tobacco smoke in utero, and mother’s prenatal use of alcoholic beverages</td>
<td>SHS exposure not associated with IQ at age 5 y (PPVT: $\beta = -0.059, P &gt; .05$; Raven: $\beta = -0.139, P &gt; .05$). SHS exposure associated with IQ scores at age 10 y (PPVT: $\beta = -1.6, P &lt; .001$; Raven: $\beta = -0.9, P &lt; .05$). Translated to 5.1 and 3.4 percentile score reductions for PPVT and Raven, respectively, for exposed compared with unexposed children.</td>
</tr>
<tr>
<td>Breslau et al. (2005) [25]</td>
<td>Longitudinal Participants recruited from a study of low and normal birth weight children United States</td>
<td>551</td>
<td>Children assessed at age 6, 11, and 17 y % female (not given) 36% exposed to SHS</td>
<td>Interview with mother at first assessment: exposure to mother’s smoking over previous 12 mo</td>
<td>IQ Wechsler Intelligence Scale for Children-Revised Wechsler Adult Intelligence Scale-third edition</td>
<td>Low birth weight, urban/suburban residence, maternal IQ, and education</td>
<td>SHS exposure associated with 2.4-point reduction in IQ scores ($P &lt; .05$) but attenuated after adjustment for maternal IQ and education ($\beta = -0.29, P &gt; .05$).</td>
</tr>
<tr>
<td>Byrd and Westman (1994) [17]</td>
<td>Cross-sectional Child Health Supplement to the National Health Survey Interview United States</td>
<td>9996</td>
<td>Age 7–17 y 49% female 41% exposed to SHS</td>
<td>Interview with parent: exposure to household smoking (exposed/not exposed)</td>
<td>History of repeating kindergarten or first grade</td>
<td>Poverty status, gender, maternal education, number of parents at home, maternal age at birth of child, race, age, severity, speech defects, enuresis, low birth weight, frequent ear infections.</td>
<td>SHS exposure associated with 40% increased risk of repeating first grade (95% CI, 1.1 to 1.7; $P = .007$). Significant interaction between SHS exposure maternal education ($\beta = -0.9; P &lt; .02$) and deafness ($\beta = -0.8; P = .01$) on risk of grade retention.</td>
</tr>
</tbody>
</table>
| Cho et al. (2010) [19]         | Cross-sectional Participants recruited from nine schools Korea | 639   | Age 8–11 y (mean 9.1 y) 48% female Mean cotinine 5.8 ng/mL, range 0.5–248.0 | Urine cotinine (continuous) | IQ, Executive function Abbreviated Korean Educational Development Institute-Wechsler Intelligence Scales; CPT; CCTT; SCWT | Age, gender, educational level of the father, maternal IQ, child IQ, residential area, birth weight, and blood lead levels | Higher cotinine levels associated with increased commission ($\beta = 0.12; P < .009$) and omission errors ($\beta = 0.15; P = .002$) and response time variability ($\beta = 0.12; P < .011$) on the CPT; lower word reading score ($\beta = 0.14; P < .002$) on the SCWT; and increased total time ($\beta = 0.12; P < .009$), and interference score ($\beta = 0.11; P < .025$) on the CCTT. SHS exposure associated with color naming and color word scores on the SCWT in unadjusted analyses only (color naming: $\beta = -1.13, P = .004$; color word: $\beta = -1.14, P = .004$). | (continued on next page)
mothers smoked but only after pregnancy (i.e., no exposure in utero) showed a 2.4-point deficit ($P > .05$) in neurodevelopmental scores compared with those whose mothers had never smoked. In a larger group, paternal smoking was significantly associated with a 3.3-point deficit in neurodevelopmental scores, but this was attenuated to a 2.4-point deficit ($P > .05$) after adjustment for maternal smoking during pregnancy [23]. Jedrychowski et al. [7] showed that years of SHS exposure was not an independent predictor of neurodevelopment after controlling for maternal education and exposure to tobacco smoke in utero at age 2 or 3 years. Only 89 of the 457 children on this study (<20%) had been exposed to SHS for any length of time and the criteria for group assignment is unclear (SHS exposure was not the primary measure in this study), so it is possible that too few children received enough SHS exposure to show a relationship with neurodevelopment.

**SHS exposure and cognition in older children**

Four cross-sectional studies investigated the relationship between postnatal SHS exposure and academic achievement. Byrd and Weitzman [17] demonstrated a 40% increased risk of early grade retention in those exposed to household SHS at the time of the survey. As some children were as old as 17 years at the time of the survey, there may have been an overestimation of the associations between SHS exposure and academic achievement if other factors associated with the grade retention led to increased family smoking after the event, although the extent to which such circumstances would attenuate these findings in such a large sample ($n = 9996$) is unclear.

Bauman et al. [16] assessed California Achievement Test performance in 973 eighth graders, demonstrating 3%–6% reductions in California Achievement Test total, language, and spelling scores with heavy exposure to household SHS, although only inverse trends were seen for mathematics and reading. Another large study by Yolton et al. [18] showed reduced reading ($-2.7$ points) and mathematics ($-1.9$ points) scores ($1 SD = 15$ points) in 6–16 year olds with high levels of cotinine, attenuated to 1.9- and 1.2-point ($P > .05$) deficits, respectively, after adjustment for SHS exposure in utero. There was also a significant 0.5-point reduction ($1 SD = 3$ points) on a measure of visuospatial ability for exposed children, but no discernible differences were seen in short-term memory. However, only the association of reading remained significant after adjustment for exposure in utero.

Cho et al. [19] measured urine cotinine concentrations in children aged 8–11 years who completed standardized Korean versions of three tasks of executive function. Increased cotinine was associated with poorer baseline and interference scores, suggesting reduced psychomotor abilities as well as an attention deficit with increasing SHS exposure (no interference deficit was seen on the Stroop test but because only errors were scored, there may have been a time-accuracy trade-off that was not identified). These findings were independent of maternal and child intelligence quotient (IQ).

Data from the prospective CHDSS study assessing the relationship between SHS exposure and intelligence was presented in two articles. Bauman et al. [20] showed no differences in intelligence at age 5 years between those exposed to SHS and those not exposed. After adjustment for variables including mother’s education level, mother’s IQ, and SHS exposure in utero, SHS exposure was associated with a 5.1-percentile score and a 3.4-percentile score deficit on the Peabody Picture Vocabulary Test and Raven’s Standard Progressive Matrices, respectively, at age 10 years. However, the conclusions drawn from the study pertaining to age were limited due to the differences in sample sizes. A second article found a linear relationship between the number of cigarettes smoked by the mother per day and reduced intelligence scores at age 5 years [4].
The relationship remained significant only for Raven’s Standard Progressive Matrices scores after adjustment for covariates including SHS exposure in utero, leading to a 2.2-point IQ deficit for children exposed to ≥20 cigarettes per day compared with children not exposed [4].

Data from a longitudinal study in the United States showed an association between SHS exposure at around age 5 years and reduced intelligence at age 6, 11, and 17 years [25]. However, this association was almost completely attenuated after adjustment for maternal IQ and education. This study compared a group of 198 children whose mothers had smoked but not during pregnancy with 353 children whose mothers had never smoked. It is unclear from the analysis in the study whether active smoking especially at 17 years of age was controlled for as this may have had an impact on IQ scores.

Discussion

This review found evidence that exposure to SHS is associated with poorer cognitive function in childhood as measured by multiple outcomes. SHS exposure in utero showed strong associations with reduced neurodevelopment especially in children aged younger than 5 years, even after controlling for postnatal SHS exposure [7,24]. Children exposed to SHS in utero still scored within normal ranges but group differences showing SHS associated with poorer cognitive function were evident. Exposure was also associated with significantly increased risk of neurodevelopmental delay [5,21]. In contrast, associations between SHS exposure in utero and IQ in older children (>5 years) were much weaker [4,6] although language and attention performance was reduced in SHS exposed children aged 6–7 years [8].

In preschool-aged children, the association between postnatal SHS exposure and neurodevelopment was generally attenuated after adjustment for prenatal SHS exposure [7,23] and other factors associated with SHS exposure such as socioeconomic status [5,7,22]. On the other hand, associations between postnatal SHS exposure and reduced intelligence and attention abilities were seen particularly in older children (>8 years) [19,20]. Measures of individual academic abilities such as reading and mathematics showed inconsistent findings [16,18], but more general measures such as grade retention and total achievement scores demonstrated substantial deficits in overall academic achievement in children exposed to SHS [16,17].

There are several potential mechanisms through which SHS may reduce level of cognitive function. SHS contains many toxic chemicals that are harmful to the brain and in utero, it can pass through the placenta from mother to fetus [26]. For example, increased concentrations of carbon monoxide into the bloodstream can impair oxygen flow to the brain [20,27,28] and nicotine acts on the cholinergic system [29,30], possibly leading to overstimulation of neurons implicated in learning and memory [29]. Five of the articles included in this review [6,7,18,19,21] examined blood lead level as a covariate. After adjustment for it, three of these studies showed a significant association between SHS exposure and cognitive parameters. Cho et al. [19] showed that adjustment for blood lead did attenuate the association of urinary cotinine and executive function performance although not to the point of nonsignificance. This suggests that lead contained within cigarettes may be responsible for at least some, but not all, of the impact of SHS exposure on cognition. Mercury was not assessed in any of the studies identified so it is unclear whether this may play a role in the associations observed.

The range of toxins contained within cigarettes could lead to effects throughout cortical and subcortical brain regions and it is therefore difficult to predict which cognitive domains and abilities may be most affected. The variety of cognitive measures used by the studies in this review makes it difficult to reconcile any differences seen in the effect of SHS exposure. Understanding the exact nature of cognitive deficits caused by SHS exposure is important for predicting long-term effects (e.g., future education attainment and socioeconomic resources) and developing timely interventions, and this should be a focus of future research. Blood measures of lead and other components of cigarette smoke such as mercury should be included in future analyses to determine the elements that have detrimental effects on the brain, which would help us to better understand the likely neurologic impacts of SHS exposure.

Several statistically significant interactions have been observed between SHS exposure and other variables, such as maternal education [17], material hardship [21], exposure to other air pollutants [6], and genetics [24]. For example, Byrd and Weitzman [17] observed a significant interaction between SHS exposure and maternal education on early grade retention (β = 0.874, P = .02). Perera et al. [6] investigated an interaction between environmental pollution and SHS exposure, showing particularly high deficits in IQ when exposure to both SHS and other pollutants were present. Individuals with other risk factors for cognitive impairment may therefore be particularly vulnerable to the physiological effects of SHS exposure and these interactions may contribute to cases of neurodevelopmental delay. On the other hand, Bauman et al. [20] did not find that those exposed to both pre- and postnatal SHS were especially vulnerable to cognitive impairment, indicating that other postnatal environmental factors may compensate for the effects of prenatal SHS exposure. Focus should be placed on identifying potential interactions to help to identify at-risk groups and to determine whether they may benefit from interventions to reduce the risk of impairment.

Self-report measures of SHS exposure may be unreliable and dichotomous coding of exposure might have resulted in insensitive group assignment, most likely biasing the findings toward the null in the case of low levels of exposure. All studies of children that used questionnaires to assess SHS exposure interviewed a parent of the participant, usually the mother, but pregnant mothers have been seen previously to underestimate their SHS exposure as indicated by cotinine levels [21,31]. However, self-reported SHS exposure can establish relative levels of exposure [32], so it should not impact greatly on group assignment for pregnant women. In addition, maternal self-reported smoking measures show reasonable reliability [18] and may lead to a relatively accurate impression of a child’s postnatal SHS exposure where there are no other significant sources of SHS. Many of the studies in this review are prospective, which to some extent reduces the risk of bias through retrospective reports of SHS exposure by mothers of children with cognitive difficulties. In our review, five studies used cotinine as a biomarker for SHS exposure, four of which demonstrated significant associations with cognitive performance [18,19,21,24]. Therefore, the findings of the association between SHS and cognitive functioning in this review are robust. In addition to the methods of SHS measurements, intensity and duration of SHS exposure from all possible sources should be measured in detail to adequately determine the dose–response relationship between SHS exposure and cognition as we have reported previously [33].

A previous review of epidemiologic studies by Eskenazi and Castorina [9] assessed the relationship between SHS exposure and cognitive, behavioral, and physical health outcomes in children. The authors identified poor control of confounding variables as a barrier to establishing an association between SHS exposure and cognition. The studies in our review controlled for several correlates of SHS exposure, such as maternal socioeconomic status, education, and age. Maternal IQ attenuated the association between SHS exposure and childhood IQ and neurodevelopment in some studies [22,25], suggesting that it is an important confounder. However, even after
adjustment for maternal IQ, the effect of SHS on cognitive executive function in children remains significant [19,24]. Only two articles [22,24] measured quality of the home environment as a covariate for analysis, but it is difficult for us to estimate what independent effect this variable had on the association between SHS exposure and cognition, although it did not appear to fully account for the association with neurodevelopment [24]. This should be explored further to determine whether postnatal environmental factors may outweigh the detrimental effects of SHS exposure, given the interactions seen between exposure and material hardship, for example [21].

It is not possible to control for all potentially confounding variables, although Eskenazi and Castorina [9] warn against over-controlling for variables that may actually lie along the causal pathway between SHS exposure and cognitive outcomes. Some studies in our review controlled for such variables including birth weight which may act as a mediating variable as has been suggested previously [11]. However, adjustment for birth weight was not found to affect the magnitude of the association between SHS exposure in utero and child neurodevelopment [5,21]. Some studies may also have “overadjusted” for covariates such as socioeconomic status by including parental income, education, and occupation [4,20]. However, again this did not appear to impact greatly on their findings or change the direction of the association, and it is therefore unlikely that residual confounding can account for the adverse effects of SHS exposure seen in these studies. Prenatal and postnatal exposures are likely to co-occur and controlling for one may lessen the perceived impact on cognition of the other, making it difficult to separate out the independent effects of each. Future research should carefully select covariates to avoid unreasonably attenuating the association between SHS exposure and cognitive functioning.

Compared with children, there are significantly fewer investigations of SHS and cognition on adults. In the UK, Llewellyn et al. [15] examined data from a cross-sectional survey, including 4809 nonsmoking men and women aged 50 years or older, and found that those who had high levels of salivary cotinine had a 44% increased risk of cognitive impairment defined by having neuropsychological test scores in the lowest 10% of the group. Increased risk of cognitive impairment remained significant even after adjustment for a number of confounders and the relationship between salivary cotinine concentration and cognitive performance was dose-dependent [15]. These findings support our review of SHS affecting early-life cognitive parameters. Because childhood intelligence and cognitive functioning are predictive of cognitive health in later life [34,35], SHS exposure during childhood may leave an individual at increased risk of cognitive impairment in later life.

The findings of this literature review are supported by recent studies that were undertaken in older populations, showing a significant “dose–response” relationship between SHS and cognitive impairment [15,36]. A limited number of studies have investigated the direct association between SHS exposure and risk of dementia and the results are inconsistent [37]. Increasingly, cognitive function in late life is viewed as the outcome of life course exposures that influence both cognitive development and cognitive decline. Early life exposures may affect cognitive function and the capacity to develop cognitive reserve. Hence, any factor that reduces potential cognitive function in young children is a potential risk factor for late-life dementia. With the world’s population aging, cognitive impairment and dementia are becoming a health care priority and SHS exposure should be investigated as a possible risk factor. Although some studies have shown beneficial effects of nicotine therapy on cognitive functioning [38,39], these studies administer nicotine directly rather than through cigarette smoking. Long-term exposure to other toxins contained within cigarettes may thus still outweigh the neural benefits of nicotine [33,40] [36].

### Conclusion

Overall, SHS exposure in utero appears important to global cognitive functioning and development over the first few years of life, whereas postnatal SHS exposure seems to become important later in childhood. SHS exposure should thus be considered a modifiable risk factor for delayed neurodevelopment and cognitive impairment. Our findings are consistent with those in studies of the effects of active smoking by pregnant women on cognitive functioning in children [14]. Given the large number of children affected by SHS exposure worldwide, these deficits may have a substantial overall impact on the wider population [10,12,13]. Based on the existing literature on this topic, we suggest that future studies should measure more exposure variables including mercury to examine the causal pathway linking tobacco smoke exposure with long-term cognitive outcomes. Public policy should continue to actively focus on reducing both pre- and postnatal exposure in an attempt to limit the health costs associated with cognitive impairment especially in later life. This may be especially pertinent in populations where SHS exposure is more common [41,42] and where other risk factors for cognitive impairment such as socioeconomic deprivation, poor cardiovascular health [37], and exposure to other air pollutants are also present [43]. At present, 93% of the world’s population still lives in countries not fully covered by smoke-free public health regulations [12]. Based on the findings of our systematic literature review, further campaigns aimed at discouraging cigarette smoking and avoiding SHS exposure could contribute to the prevention of cognitive impairment, slowing the trend of epidemic dementia worldwide.

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