Annals of Epidemiology 23 (2013) 652–661

Contents lists available at SciVerse ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

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

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ARTICLE INFO

Article history:
Received 5 November 2012
Accepted 1 July 2013
Available online 19 August 2013

Keywords:
Environmental Tobacco Smoke Pollution
Secondhand smoking
Cognition
Intelligence

ABSTRACT

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.

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.

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.

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.

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.

Methods

We searched Web of Knowledge, MEDLINE, Science Direct, Google Scholar, CINAHL, EMBASE, Zetoc, and Clinicaltrials.gov (date

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http://dx.doi.org/10.1016/j.annepidem.2013.07.001

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 $\leq$ 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 ($\geq$5 years) after postnatal SHS exposure ($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 $\leq$ 85).

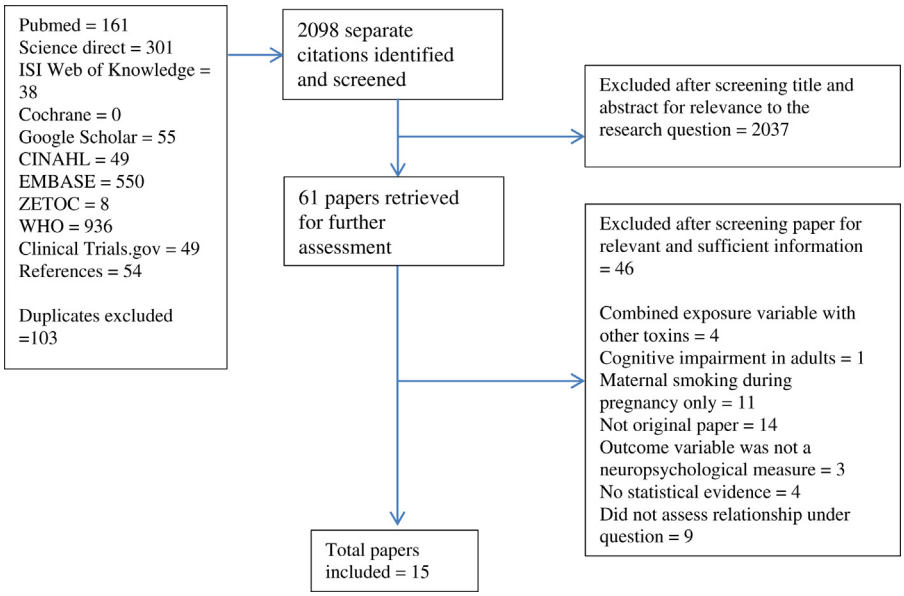

Fig. 1. Flowchart showing the process of identifying studies for this review.

Table 1
Details of studies investigating the association between SHS exposure *in utero* and cognitive functioning

First author (publication year)	Methodology, sample, and location	*N*	Population/sample characteristics	Measurement of passive smoking *in utero*	Measures of cognitive functioning	Confounders measured	Outcomes
Eskenazi and Trupin 1995 [4]	Prospective CHDS United States	1310	Mean age 5 y at follow-up 50.5% female 5.3% exposed to SHS	Maternal serum cotinine during pregnancy (exposed/not exposed)	IQ *RCPM PPVT*	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	SHS exposure not associated with unadjusted scores on the RCPM (unexposed: mean = 10.7; 95% CI, 10.6 to 10.9; exposed: mean = 10.6; 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.
Hsieh et al. (2008) [24]	Prospective Taiwan Birth Panel Study (2004–2005) Taiwan	145	Age 2 y % female 89% exposed to SHS	Cord blood cotinine (exposed [cotinine 0.16–14 ng/mL] vs. not exposed [cotinine < 0.16])	Neurodevelopment *CDIIT*	Maternal education, maternal nationality, family income, infant gender, gestational age, HOME score, postnatal SHS exposure	SHS exposure associated with reduced CDIIT total score ($\beta = -7.89 \pm 2.48$, $P = .002$), cognitive score ($\beta = -5.4 \pm 2.56$, $P = .04$), and language score ($\beta = -7.9 \pm 2.44$, $P = .002$).
Jedrychowski et al. (2009) [7]	Prospective Participants recruited through two prenatal clinics Poland	457	Assessed at 12, 24, and 36 mo of age 49% female 26.3% exposed to SHS	Interview with mother during second and third trimester of pregnancy (average number of cigarettes smoked daily in the presence of mother during pregnancy)	Neurodevelopment *BSID-MDI*	Maternal education, parity, breastfeeding, cord blood lead, gender, postnatal SHS exposure. Interaction: blood lead × gender	Significant association between SHS exposure *in utero* and average neurodevelopment over 3 y ($\beta = -2.17$ [−4.01 to −0.34], $P = .020$)
Lee et al. (2011) [5]	Prospective Mother's and Children's Environmental Health study Korea	414	Mean age 6.36 mo 50% female 63.5% exposed to SHS	Interview with mother during pregnancy (exposed vs. not exposed)	Neurodevelopment Normal (>85) vs. delayed (≤85) *Bayley Scales of Infant Development second edition Mental Development Index*	Residential area, maternal age, prepregnancy BMI, maternal education level, income, infant gender, parity, type of breastfeeding from birth to 6 mo, and birth weight	SHS exposure associated with a 2.82-point decrease in neurodevelopmental score (−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).
Makin et al. (1991) [8]	Prospective Ottawa Prenatal Prospective Study Canada	58	Age 6–7 y 52% female 60% exposed to SHS	Interview with mother during pregnancy (exposed/not exposed)	IQ, educational attainment *Wechsler Intelligence Scale for Children*, *Wide Range Achievement Test*, *Speech and language tests (PPVT, sound blending, Test of Language Development—Primary)*	Socioeconomic status	SHS exposure associated with lower language, intelligence, and attention scores but not academic achievement (multivariate $F(9,47) = 3.6$, $P < .01$).
Perera et al. (2012) [6]	Prospective Recruited from three hospitals China	100	Age 5 y 49% female 70% exposed to SHS	Interview with the mother after delivery (hours per day exposed to SHS)	IQ *Wechsler Preschool and Primary Scale of Intelligence*	Gestational age, maternal education, cord lead, mother's age, and gender	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)

Rauh et al. (2004) [21]	Prospective Mothers recruited from maternity clinics (New York) USA	226	Mean age 24 mo 48% female 40.2% exposed to SHS	Interview with mother and cord blood cotinine (exposed vs. not exposed)	Neurodevelopment Normal vs. delayed (<80) *Bayley Scales of Infant Intelligence—Mental Development Index*	Race, gender, marital status, maternal age, prenatal environmental chemical exposure, age, birth weight, birth length, head circumference, lead and airborn polycyclic aromatic hydrocarbon exposure, gestational age, maternal education, and material hardship Interaction: Material hardship × SHS exposure.	SHS exposure associated with neurodevelopmental scores lower by 4.6 points (exposed: mean = 82.0, SD = 13.0; unexposed: mean = 86.6, SD = 12.3; $F = 7.4$, $P = .007$) SHS exposure associated with an increased risk of neurodevelopmental delay (OR, 2.36; 95% CI, 1.22 to 4.48). Interaction between SHS exposure and material hardship ($P < .05$).

BMI = body mass index; CDIIT = Comprehensive Developmental Inventory for Infants and Toddlers; PPVT = Peabody Picture Vocabulary Test; RCPM = Raven Colored Progressive Matrices; SD = standard deviation.

The sources of SHS surveyed included the home, work, and outside environment although no biomarker of SHS was obtained.

Rauh et al. [21] revealed a significant 4.8-point deficit in BSID—MDI scores in 2-year-old children whose cord blood contained moderate-to-high levels of cotinine compared with those with no or low levels. This was also associated with a 1.36-fold 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 Ile462Val 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 $^1/_3$ to $^2/_3$ standard deviation lower on six different measures of intelligence and language ($P \leq .05$) 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

First author (publication year)	Methodology and location	*N*	Population/sample characteristics	Measurement of SHS exposure	Measures of cognitive functioning	Confounders measured	Outcomes
Baghurst et al. (1992) [22]	Prospective Port Pirie Cohort Study Australia	548	Age 2 and 4 y % female (not given) 40% exposed to SHS at age 2 y; 36% exposed to SHS at age 4 y	Interview with mother: exposure to mother's smoking (exposed/not exposed)	Neurodevelopment *BSID–MDI* at age 2 y *MSCA–GCI* at age 4 y	Socioeconomic status, HOME scores, and maternal IQ (Wechsler Adult Intelligence Scale)	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: $\beta = -2.04$, $P = .52$).
Jedrychowski et al. (2009) [7]	Prospective Participants recruited through two prenatal clinics Poland	457	Assessed at 12, 24, and 36 mo of age 49% female 19.5% exposed to SHS	Interview with mother: exposure to household SHS (daily number of cigarettes)	Neurodevelopment (normal vs. delayed development) *BSID-MDI*	Maternal education, parity, breastfeeding, cord blood lead, gender, and SHS exposure *in utero*. Interaction: blood lead × gender	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; $P = .317$).
Julvez et al. (2007) [23]	Prospective Asthma Multicentre Infants Cohort Study Spain	330	Mean age 4 y % female (not given) 23% exposed to SHS	Interview with mother: exposure to mother's and father's smoking (exposed/not exposed)	Neurodevelopment *MCSA*: *Working memory Memory span Executive function Posterior functions*	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	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; $P = .12$).
Lee et al. (2011) [5]	Prospective Mother's and Children's Environmental Health study Korea	414	Mean age 6.36 mo 50% female 38.5% exposed to SHS	Interview with mother: exposure to household SHS (exposed/not exposed)	Neurodevelopment Normal (>85) versus delayed (≤85) *Bayley Scales of Infant Development second edition Mental Development Index*	Residential area, maternal age, prepregnancy BMI, maternal education level, income, infant gender, parity, type of feeding from birth to 6 mo, and birth weight	SHS exposure not associated with increased risk of delayed neurodevelopment (OR, 1.06; 95% CI, 0.54 to 2.08)

BMI = body mass index; MCSA = McCarthy Scales of Children's Abilities; MSCA–GCI = McCarthy Scales of Children's Abilities–General Cognitive Index.

Table 3
Details of studies investigating the relationship between postnatal SHS and cognitive functioning in children aged 5–17 y

First author (publication year)	Methodology and location	*N*	Population/sample characteristics	Measurement of SHS exposure	Measures of cognitive functioning	Confounders measured	Outcomes
Bauman et al. (1989) [16]	Cross-sectional Participants recruited from North Carolina Public Schools United States	973	Age approximately 13 y (eighth graders) 51% female 64% exposed to SHS	Questionnaire completed by mother: exposure to parent or sibling smoking (none, 1 cigarette to 1 pack, 1–2 packs, ≥2 packs)	Academic achievement *CAT subtests: Maths Language Reading Spelling Total score*	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	SHS exposure associated with lower CAT total score ($\beta = -5.8$; $P = .018$), language ($\beta = -7.0$; $P = .008$), and spelling ($\beta = -10.9$; $P = .001$) scores. Trends between increasing SHS exposure and lower mathematics ($\beta = -4.4$; $P = .070$) and reading ($\beta = -4.3$; $P = .093$) scores.
Bauman et al. (1991) [20]	Prospective CHDS United States	2854	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)	Interview with mother at each assessment: exposure to parent's smoking at home (exposed/not exposed; number of cigarettes per day)	IQ *Raven Standard Progressive Matrices PPVT*	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	SHS exposure not associated with IQ at age 5 y (PPVT: $\beta = -.059$, $P > .05$; Raven: $\beta = -0.139$, $P > .05$). SHS exposure associated with IQ scores at age 10 y (PPVT: $\beta = -1.6$, $P < .001$; Raven: $\beta = -0.9$, $P < .05$). Translated to 5.1 and 3.4 percentile score reductions for PPVT and Raven, respectively, for exposed compared with unexposed children.
Breslau et al. (2005) [25]	Longitudinal Participants recruited from a study of low and normal birth weight children United States	551	Children assessed at age 6, 11, and 17 y % female (not given) 36% exposed to SHS	Interview with mother at first assessment: exposure to mother's smoking over previous 12 mo	IQ *Wechsler Intelligence Scale for Children-Revised Wechsler Adult Intelligence Scale-third edition*	Low birth weight, urban/ suburban residence, maternal IQ, and education	SHS exposure associated with 2.4-point reduction in IQ scores ($P < .05$) but attenuated after adjustment for maternal IQ and education ($\beta = -0.29$, $P > .05$).
Byrd and Weitzman (1994) [17]	Cross-sectional Child Health Supplement to the National Health Survey Interview United States	9996	Age 7–17 y 49% female 41% exposed to SHS	Interview with parent: exposure to household smoking (exposed/not exposed)	History of repeating kindergarten or first grade	Poverty status, gender, maternal education, number of parents at home, maternal age at birth of child, race, age, deafness, speech defects, enuresis, low birth weight, frequent ear infections.	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 ($\beta = 0.9$; $P = .02$) and deafness ($\beta = 0.8$; $P = .01$) on risk of grade retention.
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: $\beta = -.113$, $P = .004$; color word: $\beta = .114$, $P = .004$)

(*continued on next page*)

Table 3 (*continued*)

First author (publication year)	Methodology and location	*N*	Population/sample characteristics	Measurement of SHS exposure	Measures of cognitive functioning	Confounders measured	Outcomes
Eskenazi and Trupin (1995) [4]	Prospective CHDS United States	2124	Mean age 5 y at follow-up 50.5% female 34% exposed to SHS	Interview with mother: number of cigarettes child exposed to per day (none, 1–9, 10–19, >20)	IQ *Raven Colored Progressive Matrices (RCPM)* and the *PPVT*	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	SHS exposure inversely associated with PPVT scores ($t = -2.7$, $P = .007$) but attenuated in adjusted analysis ($t = -1.5$, $P = .12$). SHS exposure inversely associated with RCPM scores in unadjusted ($t = -4.2$, $P < .001$) and adjusted analyses ($t = -2.6$, $P = .01$).
Yolton et al. (2005) [18]	Cross-sectional Third National Health and Nutrition Examination Survey (NHANES III) United States	4399	Age 6–16 y % female (not given) Mean cotinine 0.23 ng/mL	Serum cotinine: ng/mL (<0.1, 0.1–1, 1–3, 3–15)	Academic achievement, intelligence *Wide Range Achievement Test (reading and mathematics subtests); Wechsler Intelligence Scale for Children-III (block design and digit span subtests)*	Gender, race, and ethnicity, poverty index, parent educational level and marital status, region of the country, iron status, and blood lead level, tobacco smoke exposure *in utero*, birth weight, NICU stay.	High-serum cotinine levels associated with reduced maths ($\beta = -1.93$; SE = 0.70; $P \leq .01$), reading ($\beta = -2.7$; SE = 0.75; $P \leq .001$) and block design ($\beta = -0.55$; SE = 0.12; $P \leq .001$) scores but not digit span ($\beta = -0.08$; SE = 0.13; $P > .05$). All effects attenuated after adjustment for prenatal exposure except for reading score ($\beta = -1.94$; SE = 0.18; $P \leq .05$).

CAT = California Achievement Test; CCTT = Children's Color Trails Test; CPT = Continuous Performance Test; NICU, Neonatal Intensive Care Unit; PPVT = Peabody Picture Vocabulary Test; SCWT = Stroop Color Word Test.

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 CHDS 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 ($\beta = 0.874$, $P = .02$). 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 overcontrolling 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 poorer areas 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.

Acknowledgments

Acknowledgments, Competing Interests, and Funding: Dr. R.C. acknowledges financial supports from Alzheimer's Research UK (ART/PPG2007B/2) and the BUPA Foundation UK (45NOV06 and TBF-M09-05) to work on Research Program for Dementia in China. Dr. A.C. works on dementia project funded by the BUPA Foundation (Dr. R.C. is the grant holder and a principal investigator). The sponsors had no role in study design, data analysis, data interpretation, or writing of the report. The opinions expressed in this report are not necessarily those of the funders.

References

[1] U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. [Atlanta, Ga.]: 2006.

[2] Ott A, Andersen K, Dewey ME, Letenneur L, Brayne C, Copeland JRM, et al. Effect of smoking on global cognitive function in nondemented elderly. Neurology 2004;62(6):920–4. http://dx.doi.org/10.1212/01.WNL.0000115110.35610.8 [online 23 March 2004].

[3] Anstey KJ, von Sanden SC, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. Am J Epidemiol 2007;166(4):367–78. http://dx.doi.org/10.1093/aje/kwm116 [online 14 June 2007].

[4] Eskenazi B, Trupin LS. Passive and active maternal smoking during pregnancy, as measured by serum cotinine, and postnatal smoke exposure. II. Effects on neurodevelopment at age 5 years. Am J Epidemiol 1995;142(Supplement 9):S19–29. http://dx.doi.org/10.1093/aje/142.Supplement-9.s19.

[5] Lee B-E, Hong Y-C, Park H, Kim JH, Chang N, Roh Y-M, et al. Secondhand smoke exposure during pregnancy and infantile neurodevelopment. Environ Res 2011;111(4):539–44. http://dx.doi.org/10.1016/j.envres.2011.02.014 [online 12 March 2011].

[6] Perera F, Li TY, Lin C, Tang D. Effects of prenatal polycyclic aromatic hydrocarbon exposure and environmental tobacco smoke on child IQ in a Chinese cohort. Environ Res 2012;114:40–6. http://dx.doi.org/10.1016/j.envres.2011.12.011 [online 1 March 2012].

[7] Jedrychowski W, Perera F, Jankowski J, Mrozek-Budzyn D, Mroz E, Flak E, et al. Gender specific differences in neurodevelopmental effects of prenatal

exposure to very low-lead levels: the prospective cohort study in three-year olds. Early Hum Dev 2009;85(8):503–10. http://dx.doi.org/10.1016/j.earlhumdev.2009.04.006 [online 17 May 2009].
[8] Makin J, Fried PA, Watkinson B. A comparison of active and passive smoking during pregnancy: long-term effects. Neurotoxicol Teratol 1991;13(1):5–12. http://dx.doi.org/10.1016/0892-0362(91)90021-N [online 6 November 2002].
[9] Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. Environ Health Perspect 1999;107(12):991–1000.
[10] Weitzman M, Florin TA, Kavanaugh M. Prenatal tobacco and postnatal environmental tobacco smoke exposure and children's cognitive and behavioural functioning. In: Bellinger DC, editor. Human Developmental Neurotoxicology. New York: Taylor & Francis; 2006. p. 149–68.
[11] Herrmann M, King K, Weitzman M. Prenatal tobacco smoke and postnatal secondhand smoke exposure and children neurodevelopment. Curr Opin Pediatr 2008;20(2):184–90. http://dx.doi.org/10.1097/MOP.06013e3282P56165.
[12] Oberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. Lancet 2011;377(9760):139–46. http://dx.doi.org/10.1016/S0140–6736(10)61388-8 [online 26 November 2010].
[13] Royal College of Physicians. (May 2012). Parliamentary briefing: passive smoking and children. Retrieved from http://www.rcplondon.ac.uk/
[14] Clifford A, Lang L, Chen R. Effects of maternal cigarette smoking during pregnancy on cognitive parameters of children and young adults—a literature review. Neurotoxicol Teratol 2012;34(6):560–70. http://dx.doi.org/10.1016/j.ntt.2012.09.004 [online 25 September 2012].
[15] Llewellyn DJ, Lang IA, Langa KM, Naughton F, Matthews FE. Exposure to secondhand smoke and cognitive impairment in non-smokers: national cross sectional study with cotinine measurement. BMJ 2009;338:b462. http://dx.doi.org/10.1136/bmj.b462 [online 12 February 2009].
[16] Bauman KE, Koch GG, Fisher LA. Family cigarette smoking and test performance by adolescents. Health Psychology 1989;8(1):97–105. http://dx.doi.org/10.1037/0278-6133.8.1.97.
[17] Byrd RS, Weitzman ML. Predictors of early grade retention among children in the United States. Pediatrics 1994;93(3):481–7.
[18] Yolton K, Dietrich K, Auinger P, Lanphear BP, Hornung R. Exposure to environmental tobacco smoke and cognitive abilities among US children and adolescents. Environ Health Perspect 2005;113(1):98–103. http://dx.doi.org/10.1289/ehp.7210 [online 7 October 2004].
[19] Cho S-C, Kim B-N, Hong Y-C, Shin M-S, Yoo HJ, Kim J-W, et al. Effect of environmental exposure to lead and tobacco smoke on inattentive and hyperactive symptoms and neurocognitive performance in children. J Child Psychol Psychiatry 2010;51(9):1050–7. http://dx.doi.org/10.1111/j.1469–7610.2010.02250.x [online 6 April 2010].
[20] Bauman KE, Flewelling RL, LaPrelle J. Parental cigarette smoking and cognitive performance of children. Health Psychol 1991;10(4):282–8. http://dx.doi.org/10.1037/0278-6133.10.4.282.
[21] Rauh VA, Whyatt RM, Garfinkel R, Andrews H, Hoepner L, Reyes A, et al. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. Neurotoxicol Teratol 2004;26(3):373–85. http://dx.doi.org/10.1016/j.ntt.2004.01.002 [online 5 March 2004].
[22] Baghurst PA, Tong SL, Woodward A, McMichael AJ. Effects of maternal smoking upon neuropsychological development in early childhood: importance of taking account of social and environmental factors. Paediatr Perinat Epidemiol 1992;6(4):403–15. http://dx.doi.org/10.1111/j.1365-3016.1992.tb00784.x [online 28 June 2008].
[23] Julvez J, Ribas-Fitó N, Torrent M, Forns M, Garcia-Esteban R, Sunyer J. Maternal smoking habits and cognitive development of children at age 4 years in a population-based birth cohort. Int J Epidemiol 2007;36(4):825–32. http://dx.doi.org/10.1093/ije/dym107 [online 5 June 2007].
[24] Hsieh C-J, Liao H-F, Wu K-Y, Hsieh W-S, Su Y-N, Jeng S-F, et al. CYP1A1 Ile462Val and GSTT1 modify the effect of cord blood cotinine on neurodevelopment at 2 years of age. Neurotoxicology 2008;29(5):839–45. http://dx.doi.org/10.1016/j.neuro.2008.05.006 [online 3 June 2008].
[25] Breslau N, Paneth N, Lucia VC, Paneth-Pollak R. Maternal smoking during pregnancy and offspring IQ. Int J Epidemiol 2005;34(5):1047–53. http://dx.doi.org/10.1093/ije/dyi163 [online 5 August 2005].
[26] Dempsey DA, Benowitz NL. Risks and benefits of nicotine to aid smoking cessation in pregnancy. Drug Saf 2001;24(4):277–322. http://dx.doi.org/10.2165/000020/8-200124040-00005.
[27] Dolan MC. Carbon monoxide poisoning. Can Med Assoc J 1985;133:392–9.
[28] Mezzacappa E, Buckner JC, Earls F. Prenatal cigarette exposure and infant learning stimulation as predictors of cognitive control in childhood. Dev Sci 2011;14(4):881–91. http://dx.doi.org/10.1111/j.1467–7687.2011.01038.x [online 23 March 2011].
[29] Slotkin TA. Developmental cholinotoxicants: nicotine and chlorpyrifos. Environ Health Perspect 1999;107(Supplement 1):71–80.
[30] Slotkin TA. Cholinergic systems in brain development and disruption by neurotoxicants: nicotine, environmental tobacco smoke, organophosphates. Toxicol Appl Pharmacol 2004;198(2):132–51. http://dx.doi.org/10.1016/j.taap.2003.06.001 [online 16 March 2004].
[31] DeLorenze GN, Kharrazi M, Kaufman FL, Eskenazi B, Bernert JT. Exposure to environmental tobacco smoke in pregnant women: the association between self-report and serum cotinine. Environ Res 2002;90(1):21–32. http://dx.doi.org/10.1006/enrs.2001.4380 [online 30 September 2002].
[32] Nondahl DM, Cruickshanks KJ, Schubert CR. A questionnaire for assessing environmental tobacco smoke exposure. Environ Res 2005;97(1):76–82. http://dx.doi.org/10.1016/j.envres.2004.02.005 [online 28 March 2004].
[33] Chen R. Association of environmental tobacco smoke with dementia and Alzheimer's disease among never smokers. Alzheimers Dement 2012;8(6):590–5. http://dx.doi.org/10.1016/j.jalz.2011.09.231 [online 23 December 2011].
[34] Fritsch T, Smyth KA, McClendon MJ, Ogrocki PK, Santillan C, Larsen JD, et al. Associations between dementia/mild cognitive impairment and cognitive performance and activity levels in youth. J Am Geriatr Soc 2005;53(7):1191–6. http://dx.doi.org/10.1111/j.1532–5415.2005.53361.x [online 29 May 2005].
[35] Whalley LJ, Starr JM, Athwas R, Hunter D, Pattie A, Deary J. Childhood mental ability and dementia. Neurology 2000;55(10):1455–9. http://dx.doi.org/10.1212/WNL.55.10.1455.
[36] Chen R, Zhang D, Chen Y, Hu Z, Wilson K. Passive smoking and risk of cognitive impairment in women who never smoke. Arch Intern Med 2012;172(3):271–3. http://dx.doi.org/10.1001/archinternmed.2011.762.
[37] Barnes DE, Haight TJ, Mehta KM, Carlson MC, Kuller LH, Tager IB. Secondhand smoke, vascular disease, and dementia incidence: findings from the cardiovascular health cognition study. Am J Epidemiol 2010;171(3):292–302. http://dx.doi.org/10.1093/aje/kwp376 [online 5 January 2010].
[38] Newhouse P, Kellar K, Aisen P, White H, Wesnes K, Coderre E, et al. Nicotine treatment of mild cognitive impairment: a 6-month double-blind pilot clinical trial. Neurology 2012;78(2):91–101. http://dx.doi.org/10.1212/WNL.0b013e31823efcbb [online 10 January 2012].
[39] White HK, Levin ED. Four-week nicotine skin patch treatment effects on cognitive performance in Alzheimer's disease. Psychopharmacology (Berl) 1999;143(2):158–65.
[40] Chen R, Wilson K, Chen Y, Zhang D, Qin X, He M, et al. Association between environmental tobacco smoke exposure and dementia syndromes. Occup Environ Med 2013;70(1):63–9. http://dx.doi.org/10.1136/oemed-2012-100785 [online 26 October 2012].
[41] King K, Martynenko M, Bergman MH, Liu Y-H, Winickoff JP, Weitzman M. Family composition and children's exposure to adult smokers in their homes. Pediatrics 2009;123(4):e559–64. http://dx.doi.org/10.1542/peds.2008-2317.
[42] Gartner CE, Hall WD. Is the socioeconomic gap in childhood exposure to secondhand smoke widening or narrowing? Tob Control 2012. http://dx.doi.org/10.1136/tobaccocontrol-2011-050297. Epub ahead of print, [online 30 March 2012].
[43] Weuve J, Puett RC, Schwartz J, Yanosky JD, Laden F, Grodstein F. Exposure to particulate air pollution and cognitive decline in older women. Arch Intern Med 2012;172(3):219–27. http://dx.doi.org/10.1001/archinternmed.2011.683 [online 13 February 2012].