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Associations Between Prenatal Cigarette Smoke Exposure and Externalized Behaviors at School Age Among Inuit Children Exposed to Environmental Contaminants

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Abstract

Background—Smoking during pregnancy is common among Inuit women from the Canadian Arctic. Yet, prenatal cigarette smoke exposure (PCSE) is seen as a major risk factor for childhood behavior problems. Recent data also suggest that co-exposure to neurotoxic environmental contaminants can exacerbate the effects of PCSE on behavior. This study examined the association between PCSE and behavior at school age in a sample of Inuit children from Nunavik, Québec, where co-exposure to environmental contaminants is also an important issue. Interactions with lead (Pb) and mercury (Hg), two contaminants associated with behavioral problems, were also explored.

Methods—Participants were 271 children (mean age = 11.3 years) involved in a prospective birth-cohort study. PCSE was assessed through maternal recall. Assessment of child behavior was obtained from the child's classroom teacher on the Teacher Report Form (TRF) and the Disruptive Behavior Disorders Rating Scale (DBD). Exposure to contaminants was assessed from umbilical cord and child blood samples. Other confounders were documented by maternal interview.

Results—After control for contaminants and confounders, PCSE was associated with increased externalizing behaviors and attention problems on the TRF and higher prevalence of attention deficit hyperactivity disorder (ADHD) assessed on the DBD. No interactions were found with contaminants.

Interpretation—This study extends the existing empirical evidence linking PCSE to behavioral problems in school-aged children by reporting these effects in a population where tobacco use is normative rather than marginal. Co-exposure to Pb and Hg do not appear to exacerbate tobacco effects, suggesting that these substances act independently.

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Keywords

attention deficit hyperactivity disorder; prenatal smoking; tobacco smoke; child behavior; environmental contaminants; externalizing behaviors; attention problems; Teacher Report Form

1. Introduction

Smoking is a major public health issue among Canadian aboriginal communities (Elton-Marshall et al., 2011), with a higher prevalence relative to non-aboriginal Canadian and U.S. norms. Data from the 2004 Nunavik Inuit Health Survey in Arctic Québec (a region called Nunavik) estimated the proportion of daily smokers to be about 70% of the population aged

15 years, and this proportion was even larger among women of childbearing age (Plaziac and Hamel, 2007). In a prospective birth-cohort study in Nunavik initiated by our group, about 90% of the participating Inuit women reported tobacco smoking during pregnancy (Muckle et al., 2011). Prenatal cigarette smoke exposure (PCSE) is increasingly recognized as a risk factor for behavioral problems at school age (Indredavik et al., 2007; Linnet et al., 2005). More specifically, epidemiological studies have reported significant associations between PCSE and externalizing behaviors, including symptoms of attention deficit hyperactivity disorder (ADHD), conduct disorder (CD) and oppositional defiant disorder (ODD) (Batstra et al., 2003; Braun et al., 2008; Brook et al., 2006; Kotimaa et al., 2003; Nigg and Breslau, 2007; Rückinger et al., 2010). In some studies, however, the association between PCSE and behavioral problems in children has been ambiguous due to confounding with parental characteristics, including socioeconomic status and maternal psychopathology (Agrawal et al., 2010; Roza et al., 2009). Moreover, recent studies suggest that postnatal exposure, through tobacco smoked in home, could be associated with similar problems, adding to the list of potential confounding factors (Gatzke-Kopp and Beauchaine, 2007; Rückinger et al., 2010; Tiesler et al., 2011; Twardella et al., 2010; Xu et al., 2010).

The Inuit population is also exposed to environmental neurotoxicants from their traditional diet based on hunting and fishing. We have recently reported that childhood lead (Pb) and prenatal methylmercury exposures predict increased externalizing behavior and attention problems at school age among children from Nunavik (Boucher et al., 2012). Recent data from the U.S. National Health and Nutrition Examination Survey suggest that the PCSE-child behavior association is intensified with co-exposure to Pb during childhood (Froehlich et al., 2009), although this pollutant has rarely been controlled for in studies on the adverse effects of PCSE. No study to date has examined whether co-exposure to methylmercury *in utero* can also exacerbate the effects of PCSE, although both substances could act on behavior through disruption of similar neurotransmitter systems (Li et al., 2006; Newland et al., 2008). The present study aims to answer the following questions: 1) Are the effects of PCSE on child behavior detected in a population, such as the Inuit, in which smoking is normative rather than marginal? 2) Are these effects still present when taking into account postnatal exposure to environmental tobacco smoke? 3) Do effects of exposure to environmental contaminants – especially postnatal Pb and prenatal methylmercury – exacerbate the effects of PCSE on behavior?

2. Methods

2.1 Procedures and Sample

The study participants were Inuit children from Nunavik, the portion of Québec located north of the 55th parallel, about 1,500 km from Montréal. Participants were initially recruited under the auspices of the Cord Blood Monitoring Program (1993–1998), which was designed to document prenatal exposure to environmental contaminants and nutrients in

Nunavik newborns (Dallaire et al., 2003), and/or for the Environmental Contaminants and Infant Development Study (1996–2000) (Muckle et al., 2001). Between September 2005 and February 2010, mothers were contacted by phone, provided with information about the study protocol, and invited to participate with their children in the school-age follow-up of the Nunavik Child Development Study. Inclusion criteria were age between 8.0 and 15.0 years, birth weight ≥ 2.5 kg, gestation duration > 35 weeks, no major birth defects, and no major neurological or health problems or pervasive development disorders. Written informed consent was obtained from a parent; oral assent, from each child. The research was approved by the Laval University and Wayne State University ethics committees.

Neurocognitive assessments were conducted on 294 children in the three largest Nunavik villages. Participants who resided in other communities were transported by plane to one of the larger villages for testing. A maternal interview was conducted to provide information on demographic background and smoking, alcohol and drug use during pregnancy. Maternal tobacco use during pregnancy was documented for 286 participants. Questionnaires were provided to the child's classroom teacher. Questionnaires from eight participants were not returned, two children were not assessed because they did not attend to school, and five were excluded for medical conditions (two with a history of epilepsy, one with a history of head trauma requiring surgery, one with a history of meningitis associated with coma and one with multiple sclerosis), for a final sample of 271.

2.2 Behavior Assessments

The Teacher Report Form (TRF; Achenbach, 1991) from the Child Behavior Checklist was completed by the child's classroom teacher. The TRF contains 112 items, each of which is rated on a 3-point scale: 0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true. Of the eight syndrome scores and three problems scores computed from specific items, this study focused on Internalizing problems, Externalizing problems, and Attention problems. Because no normative data are available for Inuit children, raw scores for each individual scale were used in statistical analyses.

The Disruptive Behavior Disorders Rating Scale (DBD; Pelham et al., 1992) contains 45 behavioral descriptors based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association 1994). It is designed to be administered to parents and teachers to provide information required for four clinical diagnoses: ADHD – inattentive type, ADHD – hyperactive-impulsive type, ODD, and CD. Each behavioral descriptor is rated on a 4-point scale: 1 = never/rarely; 2 = sometimes; 3 = often; 4 = very often. Symptoms are considered to be present when rated either 3 or 4. Clinical diagnostic criteria are met when a child presents 6 DSM-IV symptoms for ADHD – Inattentive type, 6 for ADHD – Hyperactive-impulsive type, 4 for ODD, 3 for CD. Because most (93 %) children identified as CD were also identified as ODD, children meeting criteria for either of these diagnoses were grouped together in the statistical analyses. The two ADHD categories were also grouped together to form a general ADHD measure.

2.3 Exposure to Tobacco Smoke

Maternal recall of smoking during pregnancy (yes/no) was assessed during the interview. When data on maternal substance use during pregnancy were available from previous assessments conducted at 1-month postpartum ($n = 70$) or at 5 years ($n = 89$), the information obtained closest to delivery was used to maximize the accuracy of responses. Correlations of current maternal reports of smoking during pregnancy with previous reports were strong (with 1-mo postpartum: $r = 0.80$, $p < 0.001$; with 5-year assessment: $r = 0.61$, $p < 0.001$), supporting the validity of the maternal reports provided a decade after delivery.

Postnatal environmental exposure (yes/no) was estimated by asking the mother if at least one person smoked tobacco inside the house.

2.4 Environmental Contaminant Analyses

Umbilical cord and child blood samples were analysed for concentrations of Pb, mercury (Hg), and polychlorinated biphenyls (PCBs). A blood sample (30 mL) obtained from the umbilical cord was used to indicate prenatal exposure, and a venous blood sample (20 mL) obtained from each child was used to document body burden at time of testing. Contaminant analyses were performed at the Centre de Toxicologie, Institut National de Santé Publique du Québec (Québec, Canada). Details regarding contaminants quantification in biological samples have been described elsewhere (Boucher et al., 2012).

2.5 Confounding Variables

The following potential confounding variables which have previously been shown to predict ADHD and/or other behavioral problems at school age were treated as obligatory covariates: child age and gender (Pastor and Reuben, 2008), socioeconomic status (SES) (Froehlich et al., 2007; Hollingshead, 1975), and age of the biological mother at birth (Claycomb et al., 2004). Other covariates were also documented and were identified as additional potential confounders for a supplementary set of statistical analyses: birth weight, duration of gestation, adoption status (yes/no), breast-feeding status (yes/no), parity of biological mother before child's birth, marital status (single vs. married/living with partner), nonverbal reasoning ability from principal caregiver (Raven Progressive Matrices; Raven et al., 1992), residential crowding (number of persons living in the house per room), food insecurity (mother reporting at least 1 day without sufficient food or funds to purchase food in the month preceding the study), binge alcohol drinking (at least one episode of 5 standard alcohol drinks; yes/no) and marijuana (yes/no) consumption during pregnancy, cord and current blood concentrations of Hg and Pb, and cord and current plasma concentrations of polychlorinated biphenyls congener 153 (PCB 153), and of docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid associated with beneficial effects on cognitive and behavioral outcomes (Boucher et al., 2011; Kohlboeck et al., 2011).

2.6 Statistical Analyses

Normality of distribution was inspected visually for each variable and checked for skewness (normality range: -2.0 to 2.0). The contaminant and TRF variables were log transformed since they exhibited log-normal distributions. Covariates with extreme values (>3 standard deviations from the mean) were recoded to one point greater than the highest observed non-outlying value (Winer, 1971).

The relation of PCSE to the TRF continuous scores and to the DBD dichotomous scores was examined using linear and logistic regression analysis, respectively. The obligatory covariates were included in both sets of multivariate analyses. Contaminant exposure measures associated at $p < 0.15$ with a given outcome were included in the regression analyses for that outcome; contaminant concentrations were divided into tertiles for the logistic regression analyses. Analysis of any outcomes related to prenatal binge alcohol and/or marijuana exposure at $p < 0.15$ was re-run in separate analyses including those covariates on the children for whom those data were available. In a second set of analyses, postnatal environmental tobacco smoke exposure was added to the model in order to see its contribution to the effects attributed to PCSE. Finally, for each outcome significantly associated with PCSE, interactions with contaminants were examined in exploratory analyses by adding the interaction terms (i.e., PCSE by cord Hg; PCSE by child Pb) in separate analyses. The linear regression analyses for the relation of PCSE to the TRF outcomes were also run separately for high and low exposure to the two contaminants (split

at the median). This was not done for DBD-based diagnoses because the sample size was too small when divided in two subsamples to perform logistic regression analyses.

Each statistical analysis for the relation of PCSE to child behavior was also rerun in a supplementary set of analyses in which covariates were selected using a backward selection procedure with a $p < 0.20$ cut-off level (Budtz-Jørgensen et al., 2007). All potential confounders were first included in a single regression model predicting a given outcome. Then, the covariate showing the weakest association with the outcome in question was removed from the model. This procedure was repeated until each covariate in the model was associated with the outcome at $p < 0.20$. When prenatal binge alcohol and/or marijuana exposure met criterion for inclusion in a model, this model was re-run separately with these covariables on the children for whom those data were available. Since very similar findings were obtained with this alternative approach of confounder selection, results obtained with this approach for covariable selection are reported in Supplemental material.

3. Results

3.1 Sample Characteristics

Smoking during pregnancy was common within our sample; more than 80% of the children were prenatally exposed to tobacco smoke (Table 1). Compared to women who did not smoke during pregnancy, those who smoked had lower education ($F_{(1,268)} = 3.77, p = 0.05$) and SES scores ($F_{(1,269)} = 5.72, p = 0.02$). They were also more likely to report at least one episode of binge alcohol drinking ($\chi^2_{(1)} = 5.63, p = 0.02$) and marijuana use ($\chi^2_{(1)} = 6.55, p = 0.01$) during pregnancy. Children with PCSE had lower birth weight ($F_{(1,268)} = 5.22, p = 0.02$) and higher cord Hg ($F_{(1,260)} = 6.05, p = 0.02$) and Pb ($F_{(1,260)} = 5.14, p = 0.02$) concentrations than nonexposed children. The relatively low (33%) exposure to environmental tobacco smoke in the house compared to prenatal exposure can be explained by the fact that many Inuit use their house's furnace room as a smoking room. Raw and T-scores from the TRF are presented in Table 1. *In normative samples, mean T-scores of TRF syndrome scales are 50 with one standard deviation of 10. Thus, the proportion of study children with T-scores two standard deviations above the mean is 20.8% for rule-breaking behavior, 17.8% for aggressive behavior and 4.8% for attention problems.*

3.2 Relation of PCSE to Behavioral Problems

Results from the regression analyses examining the relation of PCSE to indicators of behavioral problems are presented in Table 2. Multiple regression analyses revealed significant associations with TRF scores after statistical control for confounders and environmental contaminants. Children of mothers who smoked tobacco during their pregnancy had significantly higher scores of externalizing and attention problems. The two syndrome scales that are summed to compute the Externalizing problems scale, i.e., Aggressive behavior and Rule-breaking behavior, were also higher in these children. All these associations remained significant when binge alcohol drinking or marijuana consumption during pregnancy were included as covariates (data not shown).

Logistic regression analyses conducted with the dichotomous DSM-IV-oriented variables from the DBD revealed that children prenatally exposed to tobacco smoke are at significantly increased risk for exhibiting classroom behaviors characteristic of ADHD. Although a similar trend was observed for CD and/or ODD diagnoses, this relation did not reach statistical significance after control for confounders and environmental contaminants. When both pre- and postnatal tobacco exposure were simultaneously entered, all results with PCSE remained essentially the same, with the exception of the association with DBD-based ADHD, which fell short of statistical significance. Postnatal exposure tended to be

associated with greater attention problems, but showed no association with the other outcomes.

Table 3 presents the results of the regression analyses testing for associations between PCSE and behavior according to level of exposure to contaminants. Testing for interaction effects did not reveal any pattern of synergistic effects between PCSE and contaminants: none of the interaction terms was statistically significant (all $ps > 0.15$).

4. Discussion

This study examined the relation of PCSE to child behavioral problems at school age in a sample of Inuit children simultaneously exposed to other neurotoxic chemicals. PCSE was associated with higher scores of externalizing problems, aggressive behavior, rule-breaking behavior and attention problems, and with an increased risk of displaying the behaviors that meet the DSM-IV diagnostic criteria for ADHD as reported by the child's classroom teacher. Most effects remained significant after statistical control for sociodemographic factors, postnatal environmental tobacco smoke and exposure to other neurotoxicants, and were not exacerbated by co-exposure to environmental contaminants.

The finding of an association between PCSE and externalizing behavioral problems is consistent with data from recent studies reporting an increased risk of delinquent and aggressive behaviors among school-aged children prenatally exposed to tobacco smoke (Brook et al., 2006; Cornelius et al., 2011; Robinson et al., 2010; Rückinger et al., 2010). Other studies also found an association between PCSE and ADHD-like behaviors (Froehlich et al., 2009; Obel et al., 2009; Rückinger et al., 2010), although with somewhat less consistency. Most studies that failed to observe a significant association between PCSE and ADHD depended on parental reports of child behavior or on child retrospective report for ADHD classification (Agrawal et al., 2010; Ball et al., 2010; Cornelius et al., 2011; D'Onofrio et al., 2008; Roza et al., 2009). The present study benefited from classroom teachers' reports. Apart from constituting an independent source of observation with no awareness of the child's PCSE status, the teacher is in a unique position to compare the behavioral traits that characterize these behavior problems across children, and the elementary school classroom is an optimal observation context.

The present study adds to the existing evidence that PCSE leads to behavioral problems by reporting associations while taking into account confounders related to exposure to multiple neurotoxicants as well as sociodemographic characteristics of families and personal characteristics of the child's caregiver. Contrarily to findings from the National Health and Nutrition Examination Survey (Froehlich et al., 2009), we found no interaction between PCSE and postnatal Pb exposure on behavior problems. Indeed, associations between PCSE and behavior were very similar in the subgroup of children with low Pb exposure to those in the subgroup with higher exposure. Testing for interactions in multiple regression should be seen as exploratory due to the likelihood of limited statistical power when conducting this type of analysis in an epidemiological study (Jacobson & Jacobson, 2005; McClelland & Judd, 2003). Nevertheless, a possibility is that prenatal tobacco and Pb exposures are associated with different factors in the Inuit and in the general American population: factors specifically associated with these exposures in the latter group might account for the interaction effect previously reported. The present paper was also the first to examine interaction effects between PCSE and prenatal Hg exposure, and suggests that no such interaction occurs.

The relation of PCSE to externalizing behaviors in children is also supported by results from experimental studies showing increased hyperactivity and impaired inhibitory control in pups exposed to nicotine during gestation (Paz et al., 2007; Schneider et al., 2012). After its

entry in the foetal blood circulation, nicotine binds with nicotinic acetylcholine receptors and influences the expression of many neurotransmitters in the central and peripheral nervous systems, including acetylcholine, dopamine, norepinephrine, epinephrine and serotonin (Shea and Steiner, 2008). Although the mechanisms that underlie the associations between PCSE and behavioral problems are still unclear, it is likely that the risk of behavioral problems is increased by the influence of nicotine on the catecholamines (epinephrine, dopamine and norepinephrine), which play important roles in behaviors like impulsivity and attention (Newland et al., 2008; Ansten and Li, 2005; Arnsten, 2006).

One limitation of this study is the reliance on maternal retrospective report of PCSE in documenting maternal cigarette smoking during pregnancy. Our study could have benefited from biomarkers of cigarette smoke exposure, such as serum cotinine (e.g., Pichini et al., 2000). Nevertheless, other studies have demonstrated the validity of maternal self-reported of PCSE in relation to serum cotinine levels (Gnattingius, 2004). Furthermore, the strong correlation obtained between retrospective maternal reports at testing and at 1-month postpartum supports the validity of our PCSE indicator. However, reliance on retrospective maternal recall prevented us from quantifying the severity of PCSE given the relatively poor reliability of maternal recall of average cigarettes per day during pregnancy (Pickett et al., 2009). The absence of quantification of PCSE also precludes any dose-response analysis.

Although many confounders, including exposure to other neurotoxic agents and sociodemographic characteristics of families, have been accounted for, this study lacked information on parental psychiatric symptoms. It has been suggested that maternal and paternal antisocial characteristics as well as maternal delinquency during adolescence could potentially confound the relation between PCSE and child externalizing behaviours (Maughan et al., 2004; Silberg et al., 2003). For example, in a recent study, the association between PCSE and ADHD was explained by maternal history of ADHD (Agrawal et al., 2010). As ADHD, which is known to be highly heritable, has been associated with smoking behaviour in other populations (Kollins et al., 2005), there is a possibility that the association between PCSE and ADHD is attributable to genetic factors. Because ADHD was rarely recognized in the previous generation in Nunavik, potential confounding by parental ADHD could not be reliably assessed, as once one reaches adulthood, ADHD symptoms usually disappear. Additionally, the cultural differences in understanding mental illnesses and the limited availability of psychiatric services makes difficult to rely on medical files and diagnosis for consideration other parental psychopathology in this population. Although we, therefore, cannot rule out some contribution of parental characteristics or psychopathology associated with tobacco smoking in the relation to behavioral problems in children in our sample, a selection effect, in which women continuing smoking while pregnant would themselves be characterised by externalizing behaviour, is less likely in a study population where the large majority of the mothers smoked while pregnant. Nevertheless, additional studies examining the influence of genetic factors on the relation of PCSE to behavioural problems in children are needed to explore this hypothesis more directly. Several studies have implicated interactions between PCSE and catecholaminergic and serotonergic genes as risk factors for later child externalizing problems (Cents et al., 2012; Kahn et al., 2003; Neuman et al., 2007). Additional studies exploring family and social environment factors associated with PCSE are also needed. One recent study found no difference in conduct and oppositional problems when children were compared to their siblings who differed in exposure to PCSE, suggesting that the association between PCSE and externalizing problems found in other studies is attributable, at least in part, to environmental influences that vary among families (D'Onofrio et al., 2008).

This study replicated findings from previous studies reporting an association between PCSE and externalized behaviors and ADHD in a sample of school-aged children from Nunavik.

Findings add to the existing literature by reporting these effects in a unique population where tobacco consumption is highly prevalent. Moreover, given the occurrence of co-exposure to environmental neurotoxins in this population, interactions between PCSE and these chemicals were examined, but neither postnatal Pb nor prenatal Hg exposures was found to modify the effects of PCSE on behavior, suggesting that these substances act independently. Our results support the need for local interventions aimed to reduce PCSE among the Canadian Inuit.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ADHD	Attention deficit/Hyperactivity Disorder
CD	Conduct Disorder
DBD	Behavior Disorders Rating Scale
Hg	Mercury
ODD	Oppositional Defiant Disorder
Pb	Lead
PCSE	prenatal cigarette smoke exposure
SES	Socio-economic status
TRF	Teacher Report Form

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Highlights

- Association between prenatal cigarette smoke exposure (PCSE) and behavior is studied.
- Interactions with lead and mercury are explored.
- PCSE is associated with increased externalizing behaviors and attention problems.
- PCSE is also associated with higher prevalence of ADHD.
- Co-exposure to lead and mercury does not exacerbate tobacco effects.

Table 1

Descriptive characteristics of the study sample.

Variables	N	Mean	Median	S.D.	Range	%
Child characteristics						
Child age at assessment (years)	271	11.3	11.4	0.8	8.5 – 14.3	
Child sex (% girls)	271					50.6
Birth weight (kg)	270	3.5	3.5	0.5	2.5 – 4.7	
Duration of gestation (weeks)	271	39.2	39.0	1.4	35.0 – 44.0	
Breastfeeding status (% yes)	265					75.8
Primary caregiver characteristics/family environment						
Maternal age at delivery (years)	271	23.7	22.5	5.6	15.0 – 42.0	
Parity before child's birth	271	2.0	2.0	1.8	0.0 – 9.0	
Marital status (% single)	270					27.4
Hollingshead score ^a						
Education (years of schooling)	270	8.5	9.0	2.4	0.0 – 15.0	
Employment (% working)	269					71.7
Language at interview (% primarily Inuktitut)	271					9.6
Maternal consumption during pregnancy						
Tobacco smoke (% yes)	271					84.5
Binge drinking of alcohol (% yes) ^b	238					34.5
Marijuana (% yes)	240					30.0
11-year exposure to environmental tobacco smoke (% yes)	268					32.8
Contaminants						
Cord Pb (µg/dL)	262	4.6	3.7	3.1	0.8 – 17.8	
Current Pb (µg/dL)	267	2.7	2.0	2.2	0.4 – 12.8	
Cord Hg (µg/L)	262	21.5	16.7	17.5	1.0 – 99.3	
Current Hg (µg/L)	267	4.6	3.0	4.7	0.1 – 34.1	
Cord PCB congener 153 (µg/kg fat)	260	122.5	90.1	101.6	9.7 – 653.6	
Current PCB congener 153 (µg/kg fat)	266	74.4	45.9	84.4	3.5 – 809.5	
Teacher Report Form (raw scores)						
Externalizing problems	269	15.1	12.0	13.4	0.0 – 53.0	

Variables	N	Mean	Median	S.D.	Range	%
Aggressive behavior	269	10.1	7.0	9.6	0.0 – 38.0	
Rule-Breaking behavior	269	5.0	4.0	4.5	0.0 – 18.0	
Attention problems	269	13.8	12.0	10.9	0.0 – 42.0	
Teacher Report Form (T scores)						
Externalizing problems	269	62.3	62.0	11.0	41.0–91.0	
Aggressive behavior	269	62.4	61.0	10.4	50.0–97.0	
Rule-Breaking behavior	269	63.0	62.0	10.0	50.0–89.0	
Attention problems	269	57.2	56.0	7.3	50.0–87.0	
Teacher DBD (% meeting diagnostic criteria)						
ADHD	271					21.4
ODD and/or CD	271					22.1

^aHollingshead (1975);

^bBinge drinking corresponds to consumption of 5 standard drinks or more per occasion, one standard drink corresponding to 0.5 oz of absolute alcohol, which is equivalent to 350 ml of beer (12 oz), 175 ml of wine (6 oz), or 44 ml of liquor (1.5 oz).

Table 2

Prediction of behaviour problems at 11y by prenatal and postnatal cigarette smoke exposure in total sample.

	Prenatal exposure alone				Postnatal exposure alone				Prenatal + postnatal exposures			
	Prenatal exposure alone		Postnatal exposure alone		Prenatal exposure alone		Postnatal exposure alone		Prenatal exposure		Postnatal exposure	
	N	r	Standardized	N	r	Standardized	N	r	Standardized	N	Standardized	Standardized
TRF symptom scores (log)	256	.094	.068	253	.051	.065	253		.059	253		.066
Internalizing problems	265	.227**	.210**	262	.070	.077	262		.207**	262		.061
Externalizing problems	265	.181**	.177**	262	.067	.078	262		.176**	262		.064
Aggressive behavior	256	.228**	.188**	253	.070	.084	253		.174**	253		.069
Rule breaking behavior	256	.183**	.156*	253	.097	.130*	253		.132*	253		.133*
Attention problems												
DBD-based diagnoses	N	² (df)	AOR (95% CI)	N	² (df)	AOR (95% CI)	N		AOR (95% CI)	N		AOR (95% CI)
ADHD either type	258	5.518(1)*	3.47 (1.00–12.08)	255	1.64(1)	1.84 (0.93–3.62)	255		3.26 (0.93–11.38)	255		1.78 (0.90–3.53)
CD and/or ODD	267	3.008(1) [†]	2.14 (0.79–5.80)	264	0.83(1)	1.26 (0.67–2.38)	264		2.04 (0.75–5.56)	264		1.23 (0.65–2.31)

Values are point-biserial correlation coefficients (*r*), standardized regression coefficients () from multiple regression analyses, bivariate associations (²) and adjusted odds ratios (AOR) with 95% confidence intervals (CI) from logistic regression analyses. Adjusted models include the following obligatory covariates: child age and sex, SES, age of the biological mother at birth, and child blood Pb levels at testing. Additionally, cord Hg was included in the regression models for TRF – Internalizing Problems, TRF – Rule breaking behavior, TRF – Attention problems, and DBD – ADHD.

Table 3

Prediction of behaviour problems at 11y by maternal smoking during pregnancy according to co-exposure to contaminants

TRF symptom scores (log)	According to cord Hg				According to blood Pb						
	Low Hg (<i>n</i> = 131)		High Hg (<i>n</i> = 131)		Low Pb (<i>n</i> = 134)		High Pb (<i>n</i> = 133)				
	<i>b</i>	<i>p</i> -value	<i>b</i>	<i>p</i> -value	<i>b</i>	<i>p</i> -value	<i>b</i>	<i>p</i> -value			
Externalizing problems	.781	.272	.002	.147	.103	.680	.229	.011	.682	.205	.023
Aggressive behavior	.689	.249	.005	.372	.105	.246	.664	.227	.012	.456	.134
Rule breaking behavior	.497	.222	.011	.483	.176	.054	.297	.127	.163	.711	.280
Attention problems	.394	.147	.095	.509	.176	.051	.582	.218	.015	.280	.098

Values raw (*b*) and standardized regression coefficients () from multiple regression analyses. Adjusted models include the following obligatory covariates: child age and sex, SES, age of the biological mother at birth, and child blood Pb levels at testing. Additionally, cord Hg was included in the regression models for TRF – Internalizing problems, TRF – Rule breaking behavior, and TRF – Attention problems.