Polycyclic aromatic hydrocarbons (PAH) are a group of pollutants commonly present in ambient air from incomplete combustion of fossil fuels. They are also present in tobacco smoke (Bostrom et al. 2002) and include known carcinogens such as benzo[a]pyrene (BaP). After exposure, PAH can exert genotoxic effects, inducing mutations, as well as epigenetic effects (Perera et al. 2009). In addition, PAH bind covalently to DNA to form PAH–DNA adducts. Prenatal PAH exposure measured by personal dosimeter and behavioral/attention problems in childhood in a prospective study conducted by the Columbia Center for Children’s Environmental Health.

Objectives: We measured PAH–DNA and other bulky aromatic adducts in umbilical cord white blood cells using the 32P-postlabeling assay to determine the association between this molecular dosimeter and behavioral/attention problems in childhood.

Methods: Children born to nonsmoking African-American and Dominican women residing in New York City (NYC) were followed from in utero to 7–8 years of age. At two timepoints before 8 years of age (mean ages, 4.8 years and 7 years), child behavior was assessed using the Child Behavior Checklist (CBCL). To estimate and test the association between adducts and behavioral outcomes, both CBCL continuous raw scores and dichotomized T-scores were analyzed.

Results: Higher cord adducts were associated with higher symptom scores of Anxiety/Depression at 4.8 years and Attention Problems at 4.8 years and 7 years, and with Diagnostic and Statistical Manual of Mental Disorders, 4th edition–oriented Anxiety Problems at 4.8 years.

Conclusions: These results suggest that PAH exposure, measured by DNA adducts, may adversely affect child behavior, potentially affecting school performance.

Key words: cord blood, DNA adducts, neurodevelopment, PAH, 32P-postlabeling, Environ Health Perspect 119:1176–1181 (2011). doi:10.1289/ehp.1002705 [Online 12 April 2011]

Polycyclic aromatic hydrocarbons (PAH) are a group of pollutants commonly present in ambient air from incomplete combustion of fossil fuels. They are also present in tobacco smoke (Bostrom et al. 2002) and include known carcinogens such as benzo[a]pyrene (BaP). After exposure, PAH can exert genotoxic effects, inducing mutations, as well as epigenetic effects (Perera et al. 2009). In addition, PAH bind covalently to DNA to form adducts, a widely used indication of DNA damage that has been associated with cancer (Bartsch 1996; Poirier and Anderson 1985; Tang et al. 1995, 2002; Bostrom et al. 2002) and behavioral/attention problems in childhood (Rapport et al. 2001). In addition, higher levels of cord PAH–DNA adducts have been associated with reduced scores on neurocognitive tests, alone or in combination with environmental tobacco smoke (ETS) (Perera et al. 2006, 2007, 2009; Tang et al. 2006).

To date there have been no reports of associations between DNA adducts and child behavior. Here we have assessed the relation between cord PAH/bulky-DNA adducts and behavior problems (especially anxiety/depression and attention problems) at age 4.8 years (range 3.75–5.9 years) and age 7 years (range 6–8 years) using the age-appropriate Child Behavior Checklist (CBCL) (Achenbach and Rescorla 2000, 2001a). The CBCL has been widely used and is sensitive to diverse prenatal environmental exposures (Axtell et al. 2000; Raub et al. 2006; Robinson et al. 2008; Wasserman et al. 2001).

Methods

Sample selection. A complete description of the CCCEH NYC cohort and study design appears elsewhere (Perera et al. 2003, 2006).

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We thank the Centers for Disease Control and Prevention (Atlanta, GA) for their analysis of umbilical cord lead and polycyclic aromatic hydrocarbon metabolites in children.

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Briefly, African-American and Dominican women who resided in Washington Heights, Harlem, or the South Bronx in New York City, USA, were recruited between 1998 and 2003 into a prospective cohort study (Perera et al. 2003). To reduce the potential for confounding, we limited enrollment to women who were in the age range of 18–35 years; non–cigarette smokers; nonusers of other tobacco products or illicit drugs; free of diabetes, hypertension, or known HIV; and who initiated prenatal care by the 20th week of pregnancy. We complied with all applicable requirements of the United States, and the institutional review board of the New York Presbyterian Medical Center approved the study. All women provided written informed consent prior to study initiation and at each visit; children provided assent starting at 7 years of age.

**Personal interview and HOME inventory.** A trained bilingual interviewer administered a 45-min questionnaire during the last trimester of pregnancy to obtain demographic information, residential history, and health and environmental data such as active and passive smoking, ETS exposure was self-reported as having at least one smoker in the home, dichotomized as a yes/no variable (Perera et al. 2003). The questionnaire also elicited information on dietary PAH (consumption of broiled, fried, grilled, or smoked meat), and socioeconomic information related to income and education (Perera et al. 2003). Postnatal maternal interviews were administered in person when the child was 6 months and annually thereafter to determine any changes in residence, exposure to ETS, and other health or environmental conditions. The Home Observation for Measurement of the Environment (HOME) Inventory (Bradley 1994) was used to assess the quality of the home caretaking environment. Self-reported maternal demoralization was measured by the Psychiatric Epidemiology Research Instrument Demoralization Scale (Dohrenwend et al. 1978). We administered the Test of Nonverbal Intelligence-Second Edition (TONI-II), a language-free measure of intelligence (Brown et al. 1990; Caldwell and Bradley 1979) to the mothers at about child age 3 years.

**Biomarkers.** Umbilical cord blood (30–60 mL) was collected at delivery (Perera et al. 2004). The nuclease P1 digestion enhancement procedure of the 32P-postlabeling assay was used to analyze bulky/hydrophobic DNA adducts in umbilical cord blood samples having a sufficient yield of DNA (≥ 12 μg). The 32P-postlabeling assay is highly sensitive and can be used to detect various DNA adducts with multiple structures (Phillips and Arlt 2007). It can detect adducts in the range of one per 10^6–10^9 nucleotides using a 4-μg DNA sample. The bulky/hydrophobic DNA adducts detected by the assay include those formed by PAHs and other genotoxic carcinogens, for example, nitro-PAH and aromatic amines. In this assay, tissue DNA is degraded enzymatically to mononucleotides; these are then 32P-labeled via T4 polynucleotide kinase-catalyzed [32P]P-phosphate transfer from [γ-32P]ATP to form 5’-32P-labeled 3’,5’-bisphosphate derivatives. The labeled products are resolved by multidirectional thin-layer chromatography and detected and quantified as described (Phillips and Arlt 2007; Randerath et al. 1989). An aliquot (4 μg) of each DNA sample was analyzed on three separate occasions in batches of between 20 and 28 samples. For each assay, a positive control consisting of DNA modified with BaP diol-epoxide was also analyzed.

Lead was measured at the Centers for Disease Control and Prevention (CDC) in a subset of cord bloods (n = 153) using inductively coupled plasma mass spectrometry (CDC/Division of Laboratory Science 2003). To adjust for postnatal exposure to PAH, urinary PAH metabolites were measured in a subset of children at 5 years of age (n = 102). Urine was analyzed, as DNA from blood samples was not available for this assay and urinary PAH metabolites are a well-validated internal dosimeter for these compounds. The CDC measured a suite of 22 PAH metabolites, using enzymatic deconjugation, followed by automated liquid–liquid extraction and quantified by gas chromatography/isotope dilution high-resolution mass spectrometry (Li et al. 2008).

**Behavioral outcomes.** Research workers trained in neurodevelopmental testing administered the CBCL to the mothers, using the 99-item CBCL for children < 6 years of age (Achenbach and Rescorla 2000) and the 118-item CBCL for children ≥ 6 years (Achenbach and Rescorla 2001a). The syndrome scores were computed for each domain of a priori interest (Anxious/Depressed and Attention Problems) by summing the scores on the specific items, which yields a raw score. This raw score can be converted to a standardized T-score. We report results from two versions of the CBCL administered at two different ages: the two versions have different numbers of items and distributions of scores. T-scores were generated by the CBCL software according to the procedure of Abramowitcz and Stegun (1968). A T-score of 50 is assigned to children with percentiles of raw scores ≤ 50 based on a reference population (Achenbach and Rescorla 2000), whereas those with percentiles of raw scores > 50 are assigned the actual T-score. The CBCL also yields scales derived from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association 2000), that are intended to approximate clinical diagnoses. The DSM-IV scores are dichotomized using a borderline or clinical cut point corresponding to the 93rd percentile for each domain (Achenbach and Rescorla 2000). Based on our a priori hypothesis, we focused on the DSM-oriented Anxiety Problems in our analysis.

**Statistical methods.** Cord DNA adducts (range 0.2–24.8 adducts/10^9 nucleotides) were dichotomized at the upper quartile (2.7 adducts/10^9 nucleotides) of the 461 children with data on DNA adducts and maternal prenatal questionnaire data. Among the 215 children in the present analysis, we identified 58 and 157 subjects as high exposed and low exposed, respectively. Although the dichotomized adduct variable is our independent variable of choice, we have also used logarithm-transformed adducts as a continuous variable. Covariates were selected based on whether they were significant contributors to the model (here at p ≤ 0.1) for at least one of the outcomes. Although ethnicity (African American or Dominican) was not a significant covariate in the model, it was included because it is highly correlated with the CBCL scores and there is a significant difference in ethnicity between the subjects included and those not included. Covariates in the models included ETS exposure during pregnancy, sex of child, gestational age of the child, intelligence of mother as measured by TONI-II, completed years of education of the mother before birth of the child, age of child at assessment in months, quality of the early home caretaking environment measured at 3 years of age, and season of the last trimester (either during the heating season from 1 October to 30 April, when ambient PAH levels are higher, or not). Gestational age was based on medical record data for almost all subjects. Covariates are defined in Table 1.

With respect to CBCL syndrome scores, both the continuous raw scores and the dichotomized T-scores were analyzed. Because the raw scores of each domain of interest are counts data that sum the scores on the specific items within each syndrome scale, we applied the Poisson model on the raw scores for the syndromes. We further analyzed the syndrome T-scores dichotomized at 65 (the cutoff for scores for the borderline and clinical range) (Achenbach and Rescorla 2000) using a logistic model. We used logistic regressions for analysis of dichotomized DSM-oriented Anxiety Problems (cutoff at 93rd percentile for the borderline and clinical range).

To estimate associations between PAH and behavior outcomes at different ages, two separate analyses were done on CBCL measures at (mean) 4.8 years (n = 96) and (mean) 7 years (n = 205). Note that 86 children had measures at both time points.

To check for the possible confounding effect of postnatal PAH exposure, we fit a
separate model with CBCL measurements of children at 7 years adjusting for PAH metabolites in child urine collected at 5 years of age. Because of incomplete data on postnatal PAH exposure, the model with postnatal PAHs had a smaller sample size (n = 100 at age 7 years). Moreover, to check the possible confounding effect of postnatal ETS exposure, we fit separate models adjusting for postnatal ETS exposure measured at 2 years of age. Similarly, because of incomplete data on postnatal ETS exposure, the separate models had smaller sample sizes (n = 85 at age 4.8 years and n = 182 at age 7 years). We also fit a model that included an interaction term between adducts and sex of the child to check for possible interactions.

All effect estimates, 95% confidence intervals (CIs), and p-values (β set at 0.05) were generated using SAS (version 9.1.0.3; SAS Institute Inc., Cary, NC, USA).

Results

Four hundred sixty-one children had data on DNA adducts in cord blood as well as prenatal questionnaire data. Missing adduct data resulted from failure to collect cord blood or insufficient amounts of DNA available for the assay. Two hundred fifty-two of the children had CBCL data obtained at least once at (average) ages 4.8 years or 7 years (ranges, 3.75–5.9 and 6–8 years, respectively). The subset included in the present analysis was composed of 215 of these mother–child pairs who also had available data on all explanatory or potential confounding variables of interest. The remainder of the 461 study participants either had a CBCL measurement completed outside of the identified time period (n = 109), did not have a CBCL measurement at all (n = 100), or were missing data on key covariates (n = 37).

CCCEH NYC participants included in the present study (n = 215) were similar to participants with adduct data who were not included because of missing CBCL or covariate data (n = 246) with respect to level of cord DNA adducts and ETS exposure, gestational age, maternal education, self-reported maternal demoralization, the quality of the home caretaking environment (HOME), and season of the last trimester (Table 1). However, children included in the present analysis were more likely to be female and African American than those not included (Table 1). We also compared the 461 children with cord adducts measured by 32P-postlabeling with children lacking adduct data and found that they differed significantly only with regard to gestational age (39.68 weeks vs. 39.26 weeks, p = 0.0006).

### Table 1. Characteristics of the sample (mean ± SD or %).

| Variable | Subjects in the analysis (n = 215) | Subjects not included (n = 246) | Value | n |
|----------|-----------------------------------|---------------------------------|-------|---|
| Cord 32P adducts | 2.45 ± 2.43 | 2.32 ± 2.31 | 246 |
| Prenatal ETS | 36.28 | 34.15 | 246 |
| Female | 59.53 | 47.56 | 246 |
| Gestational age | 39.68 ± 1.49 | 39.57 ± 1.34 | 246 |
| Maternal demoralization score | 1.19 ± 0.62 | 1.16 ± 0.67 | 219 |
| Maternal education | 11.84 ± 2.18 | 11.85 ± 2.27 | 246 |
| Maternal TONI score | 20.77 ± 8.70 | 19.89 ± 8.50 | 144 |
| Home environment | 39.98 ± 6.26 | 38.62 ± 6.52 | 129 |
| Ethnicity | 44.65 | 30.08 | 246 |
| Heating season | 53.95 | 58.57 | 235 |

ASome subjects were not included because of missing CBCL or information on at least one covariate. aThe 32P-postlabeling assay was used to measure adducts. Units are adducts/106 nucleotides. bPrenatal ETS exposure in the home. cSignificantly different between the two groups based on Pearson’s chi-square test. dGestational age in weeks. 

Maternal demoralization during pregnancy. eMaternal education in years of school. fNonverbal intelligence measured by the TONI. gHOME Inventory as a measure of the home caretaking environment. hPercentage African American; the remainder are Dominican. iThird trimester in heating season.

### Table 2. Distribution of selected outcomes in the CCCEH NYC cohort.

| Mean age (range) | n | Outcome | Score range | Mean of scores | Borderline or clinical range (n)[%]
|-----------------|---|---------|-------------|---------------|----------------------------------|
| 4.8 years | 98 | Anxious/depressed | T-score T-score Raw score | 50–87 | 50–82 | 0–9 | 0–9 | 30.69 | 30.69 |
| (3.75–5.91 years) | | Attention problems | | 0–13 | 0–17 | 0–16 | 0–8 | 54.60 | 53.72 | 54.60 | 54.60 |
| | | Anxiety problems (DSM) | | 0–16 | 0–16 | 0–16 | 0–8 | 3.01 | 3.01 | 3.01 | 3.01 |
| | | Anxiety problems (DSM) | | 0–13 | 0–17 | 0–16 | 0–8 | 1.34 | 1.34 | 1.34 | 1.34 |
| 7 years | 205 | Anxious/depressed | T-score T-score Raw score | 50–87 | 50–82 | 0–9 | 0–9 | 30.69 | 30.69 |
| (6–8 years) | | Attention problems | | 0–13 | 0–17 | 0–16 | 0–8 | 54.60 | 53.72 | 54.60 | 54.60 |
| | | Anxiety problems (DSM) | | 0–16 | 0–16 | 0–16 | 0–8 | 3.01 | 3.01 | 3.01 | 3.01 |

*The T-score is truncated (Petersen et al. 1993); that is, a score of 50 is assigned to those with percentiles of raw scores ≤ 50 based on a reference population (Achenbach and Rescorla 2001b). bThe syndrome T-scores were dichotomized at T = 65 as the cutoff for the borderline and clinical range; the DSM-IV-oriented anxiety problem scale was dichotomized at 33rd percentile for the borderline and clinical range. cEighty-six children had been assessed via the CBCL at both age time points.

Table 2 provides the distribution of CBCL scores. Both raw scores and T-scores are highly right skewed. As expected, the mean scores in our study are similar to mean scores of the normative sample of children who have not been referred to mental health services or special education (Achenbach and Rescorla 2001b, 2001c). Correlation coefficients between the syndrome scores of Anxious/Depressed and Attention Problems ranged from 0.37 to 0.57.

In simple Poisson models without adjustment for covariates (data not shown), the children with higher levels of cord DNA adducts had higher scores, consistent with increased Anxious/Depressed and Attention Problems at (mean) 4.8 years and at (mean) 7 years, relative to children with lower cord DNA adduct levels. In the full Poisson model after adjusting for possible confounders, higher levels of cord DNA adducts were associated with the syndrome scores of Anxious/Depressed (β = 0.34, 95% CI, 0.04–0.64, p = 0.026) and Attention Problems (β = 0.38, 95% CI, 0.06–0.69, p = 0.018) at (mean) 4.8 years and with Attention Problems at (mean) 7 years (β = 0.22, 95% CI, 0.06 to 0.38, p = 0.009) (Table 3). The beta coefficient 0.34 of the adduct high/low variable on symptoms of Anxious/Depressed suggests that subjects in the upper quartile of adducts have about a 40% [$\exp(0.34) = 1.4$] increase in symptom scores compared with subjects with adduct levels below the 75th percentile; that is, for subjects with mean CBCL Anxious/Depressed scores of 3, those in the upper quartile will have scores 1.2 points higher, on average, than subjects who have lower adduct levels. After Bonferroni correction, the associations between cord DNA adducts and CBCL outcomes did not remain significant. However, the Bonferroni correction is considered to be overly conservative in initial studies such as this (Wacholder et al. 2004).

After controlling for postnatal exposure to ETS at 24 months, the association between DNA adducts and the syndrome score of Attention Problems became more significant at 4.8 years with a higher beta (β = 0.45, p = 0.012, n = 85) and at age 7 years (β = 0.25, p = 0.006, n = 182) and remained significant for the syndrome score of Anxious/Depressed (β = 0.37, p = 0.031, n = 85) at 4.8 years of age. After controlling for PAH metabolites in child urine collected at 5 years of age, higher cord adducts were significantly associated with the syndrome score of Attention Problems at 7 years (β = 0.28, p = 0.028, n = 100). These latter analyses involved limited numbers of subjects, so power was reduced accordingly.

As a further analysis, we used logistic regression on T-scores dichotomized at 65 for the syndrome scales (Table 3). The
results were significant for the syndromes of Attention Problems at 7 years [odds ratio (OR) = 3.30, 95% CI, 1.21–12.54] and Anxious/Depressed at 4.8 years (OR = 8.14, 95% CI, 1.21–54.94), showing that higher cord adducts were associated with increased likelihood of borderline or clinical classification on Anxious/Depressed and Attention Problems. We also used the logistic model on DSM-oriented Anxiety Problems (Table 3). The results show that higher cord adducts were associated with increased likelihood of borderline or clinical classification on the DSM-oriented Anxiety Problem Scale (OR = 8.30, 95% CI, 1.13–60.71) at 4.8 years of age.

With continuous adducts used as the main predictor, the results were consistent with those using the dichotomized cord adduct variable for Attention Problems at 7 years of age; that is, they had the same direction of the association and were statistically significant (β = 0.19, p = 0.001); however, the adducts were no longer significant for age 4.8 years, not were they significant with the syndrome of Anxious/Depressed at either time point.

The use of dichotomized cord adducts is preferable because dichotomization is less vulnerable to errors in measurement, does not materially lose information, and permits comparison of the most highly exposed children with those who had lower exposure.

Correlations between cord adducts and ETS and dietary PAHs, respectively, were not significant using Spearman rank-order correlation (r = 0.05, p = 0.43) and Pearson correlation (r = −0.04, p = 0.55). The correlation between adducts and lead was also not significant in the limited subset with both measurements (by Pearson correlation: r = 0.06, p = 0.44, n = 153). Dietary PAHs and lead were not associated with outcomes at t = 0.1 and were therefore not included in the models. In addition, as stated above, we had the data for only a subset of the sample.

**Discussion**

Previous results from this cohort study have provided evidence that prenatal exposure to PAH air pollutants during pregnancy is a risk factor for developmental delay at 3 years of age, as measured by the Bayley Scales of Infant Development (Perera et al. 2006), and for reduced child IQ at 5 years. To our knowledge, there have been no prior molecular epidemiologic studies of the role of prenatal DNA adducts in child behavior. The present analysis, using bulky/hydrophobic DNA adducts detected by 32P-postlabeling analysis as a molecular dosimeter for PAHs and other combustion-related pollutants, suggests an adverse effect of those exposures on child behavioral problems that potentially could affect cognitive test scores and ability to learn. We did not observe clear differences in associations between DNA adducts on child behavioral problems among boys and girls (adduct–sex interactions were not significant in any syndrome scores at either age; all p-values > 0.6).

The associations between DNA adducts and syndromes of Attention Problems and Anxious/Depressed observed in this New York City population are consistent with the experimental data on PAHs (Saunders et al. 2006; Takeda et al. 2004; Wormley et al. 2004a; Yokota et al. 2009). Prenatal treatment of rats with BaP impaired memory and ability to learn, consistent with alterations in the expression profile of key genes involved in long-term potentiation (Hood et al. 2000; Wormley et al. 2004b). Fetal BaP exposure also influenced the expression of nuclear transcription factors that mediate the onset of neuronal cell differentiation, suggesting that there may be widespread effects of this agent in the developing brain, ultimately contributing to neurobehavioral impairment (Hood et al. 2000).

The mechanisms by which PAHs might affect the developing brain are not fully known. Fetal toxicity may be caused by endocrine disruption (Archibong et al. 2002; Bui et al. 1986; Takeda et al. 2004), binding to receptors for placental growth factors resulting in decreased exchange of oxygen and nutrients (Dejmek et al. 2000), binding to the human Ah receptor to induce P450 enzymes (Manchester et al. 1987), DNA damage resulting in activation of apoptotic pathways (Meyn 1995; Nicol et al. 1995; Wood and Youle 1995), epigenetic effects (Wilson and Jones 1983), or oxidative stress due to inhibition of the brain antioxidant scavenging system (Lundqvist et al. 2006). The prenatal period is highly sensitive to neurotoxic effects of environmental contaminants (Nijland et al. 2008; Rodier 2004).

In our cohort, DNA adducts were associated with CBCL test scores consistent with increased attention problems at 4.8 and 7 years of age and increased anxiety and depression scores at 4.8 years of age. Attention problems at 6 years of age have been associated with achievement in high school; this may be due to children never fully grasping elementary concepts, making comprehending more complex ideas very challenging (Breslau et al. 2009). Prior research has shown that internalizing behavioral problems may lead to a wide range of learning deficits in areas ranging from problem-solving tasks to verbal memory to intellectual function (Emerson et al. 2005; Gunther et al. 2004; Lundy et al. 2010). Finally, attentional and internalizing problems are worrisome outside the academic domain as well. Attention deficits and anxious and depressive behaviors are linked to difficulties in peer relationships and other social functioning (Alfano and Gamble 2009; Edsbyn et al. 2010; Ladd 1999; Swords et al. 2011). The children in our cohort are being followed to 12 years of age; therefore, subsequent testing will provide a picture of the longer-term developmental outcomes of children in the cohort.

The strengths of the analysis include our ability to account for a number of factors other than PAH exposure that are known to affect child behaviors. We were able to draw upon individual prenatal exposure data from personal monitoring, biomarker data, and extensive medical record and questionnaire data. A limitation of this research is our relatively small sample size of the subjects in the analysis. This attrition is attributable to the exclusion of subjects who are missing complete covariate data or testing results. There is a possible effect of selection bias, because there is a difference in the sex and ethnicity distribution of the included and excluded subjects. Another limitation is the reduced number of children with lead measurements, limiting interpretation of analyses controlling for lead exposure.

**Table 3.** Associations between DNA adducts in cord blood and CBCL syndrome and DSM-oriented outcomes.6

| Exposure | CBCL: Anxious/depressed | CBCL: Attention problems | DSM: Anxiety problems |
|----------|-------------------------|--------------------------|----------------------|
|          | Poisson raw             | Logistic dichotomized T  | Poisson raw         | Logistic dichotomized T | Logistic model |
|          | β (95% CI)              | p-Value                  | OR (95% CI)         | p-Value                  | OR (95% CI)     | p-Value |
| Cord 32P adds, age 4.8 yearsb,c | 0.34 (0.04–0.64) | 0.026* | 8.14 (1.21–54.94) | 0.031* | 0.38 (0.06–0.69) | 0.018* | 5.66 (0.64–50.05) | 0.119 | 8.30 (1.13–60.71) | 0.037* |
| Cord 32P adds, age 7 yearsd,e | −0.03 (−0.22 to 0.16) | 0.773 | 1.42 (0.45–4.46) | 0.544 | 0.22 (0.06–0.38) | 0.009* | 3.30 (1.22–12.54) | 0.022* | 1.26 (0.42–3.82) | 0.683 |

6The model includes prenatal ETS, sex of child, gestational age, maternal IQ, HOME inventory, maternal education, ethnicity, prenatal demoralization, age at assessment, and heating season as covariates. Adducts were dichotomized at upper quartile. aRange: 3.75–5.91 years, n = 96, with 80 children classified as low exposure and 16 children classified as high exposure. bRange: 6–8 years, n = 153). Dietary PAHs and lead were not associated with outcomes at t = 0.1 and were therefore not included in the models. In addition, as stated above, we had the data for only a subset of the sample. cRange: 4.8–7 years, n = 119. dRange: 6–8 years, n = 125, with 80 children classified as low exposure and 45 children classified as high exposure. eRange: 4.8–7 years, n = 205, with 149 children classified as low exposure and 56 children classified as high exposure. *p < 0.05.
Although lead was not found to be significantly correlated with DNA adducts, CBCL, or potential confounders in the present data set, it is possible that we lack the necessary sample size to test the relationships adequately.

Conclusion

In this study, it suggests that prenatal exposure to PAHs at levels encountered in the air of New York City may adversely affect child behavior. The results are of potential concern, because attention problems and anxiety and depression may affect subsequent academic performance as well as peer relationships and other aspects of societal functioning (Emslie 2008; Esbjorn et al. 2010; Swords et al. 2011; Wood 2006). PAHs are widespread in urban environments in the United States and worldwide largely as a result of fossil fuel combustion for energy production and transportation. Fortunately, it is possible to reduce airborne PAH concentrations through currently available pollution controls, energy efficiency, alternative energy sources (Wong et al. 2004), and regulatory intervention to reduce or control pollutant sources (Millman et al. 2008).

References

Abramowitz M, Stegun IA. 1968. Handbook of Mathematical Functions. Dover, NY: Dover Publications.
Achenbach T, Rescorla L. 2000. Child Behavior Checklist for Ages 1 1/2–5. 6-1-01 Ed. Burlington, VT: Achenbach System of Empirically Based Assessment (ASEBA).
Achenbach T, Rescorla L. 2001a. Child Behavior Checklist for Preschool Forms and Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth and Families.
Achenbach T, Rescorla L. 2001b. Manual for the ASEBA Preschool Forms and Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth and Families.
Afanno CA, Gamble AL. 2009. The role of sleep in childhood psychiatric disorders. Child Youth Care Forum 38(3):327–340.
American Psychiatric Association. 2000. Task Force on DSM-IV. 2000. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR 4th ed. Washington, DC: American Psychiatric Association.
Anderson LM, Diwan BA, Fear NT, Roman E. 2000. Critical windows of exposure for children’s health: cancer in human epidemiological studies and experiments in newborn animal models. Environ Health Perspect 108(suppl 3):573–594.
Archibong AE, Inyang N, Greenwood M, Nayar T, Koppesl P, et al. 2002. Alteration of pregnancy related hormones and fetal survival in F-344 rats exposed by inhalation to benzo(a)pyrene. Reprod Toxicol 16(6):801–808.
Axtell CD, Cox C, Myers GJ, Davidson PW, Choi AL, Axtell CD, Khouw JH, Siddiqui WN, Li, Ramesh A, Sheng L, et al. 2007. Down-regulation of early ionotropic glutamate receptor subunit developmental expression as a mechanism for observed plasticity deficits following prenatal exposure to benzo(a)pyrene. Neurotoxicology 28(5):955–978.
Brown LA, Sherbenou RJ, Johnson SK. 1999. Test of Non-Verbal Intelligence: A Language-Free Measure of Cognitive Ability. 2nd ed. New York, NY: Psychological Corporation.
Bui QG, Tran MB, West WL. 1986. A comparative study of the reproductive effects of methadone and benzo(a)pyrene in the pregnant and pseudopregnant rat. Toxicology and Applied Pharmacology 86(1):23–30.
Calow BM, Bradley RH. 1979. Home Observation for Measurement of the Environment. Little Rock, AK: University of Arkansas Press.
CDC (Centers for Disease Control and Prevention) Division of Laboratory Science. 2003. Whole Blood Lead, Cadmium and Mercury Determined Using Inductively Coupled Plasma Mass Spectrometry, DLS method Code: 2003-01/OD: CIA Methods. Atlanta, GA: Centers for Disease Control and Prevention.
Dejmk J, Solansky I, Benes I, Lenecik J, Slam J. 2000. The impact of polycyclic aromatic hydrocarbons and fine particles on pregnancy outcome. Environ Health Perspect 108:1159–1164.
Dohrenwend BS, Krasnow L, Askenasy A, Dohrenwend B. 1978. Exemplification of a method for scaling life events: the PERI life events scale. J Health Soc Behav 19:205–229.
Emerson CS, Mallett GA, Harrison DW. 2005. Anxious-depression in boys: an evaluation of executive functioning. Arch Clin Neuropsychol 20(4):539–546.
Emslie GJ. 2008. Pediatric anxiety—underrecognized and undertreated. Pediatr Neurosci 34(suppl 1):283–290.
Esbjorn BH, Hoeyer M, Dyrborg J, Leth I, Kendall PC. 2010. Prevalence and co-morbidity among anxiety disorders in a national cohort of psychiatrically referred children and adolescents. J Anxiety Disord 24(6):866–872.
Grandjean P, Landrigan PJ. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368(9533):2167–2178.
Gunther T, Holtkamp K, Jolles J, Hertzog-Dahmann B, Konrad K. 2004. Verbal memory and aspects of attentional control in children and adolescents with anxiety disorders or depressive disorders. J Affect Disord 82(2-3):265–269.
Hoob DB, Nayar T, Abraham M, Greenwood M, Inyang F. 2000. Brain function and aspects of attentional control in children and adolescents with anxiety disorders or depressive disorders. J Affect Disord 82(2-3):265–269.
Hood DB, Nayar T, Abraham M, Greenwood M, Inyang F. 2000. Brain function and aspects of attentional control in children and adolescents with anxiety disorders or depressive disorders. J Affect Disord 82(2-3):265–269.
Kopsombut P, et al. 2002. Alteration of pregnancy related hormone levels in rats with perinatal benzo(a)pyrene exposure. Reprod Toxicol 16(6):801–808.
Ladd GW. 1999. Peer relationships and social competence in early and middle childhood. Annu Rev Psychol 50:337–365.
Li Z, Sandau CD, Romanoff LC, Caudill SP, Sjiddon A, Needham LL, et al. 2008. Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population. Environ Res 107(1):320–331.
Lundqvist C, Besinger M, Ljungs M, Johansson C, Coccalletti S, Saunders M, et al. 2006. The effects of PCBs and dioxins on child health. Acta Paediatr 95(suppl 935):55–64.
Lundqvist SM, Silva GE, Kaemingk KL, Goodwin JL, Quan SF. 2000. Pediatric mental animal models. Environ Health Perspect 108(suppl 3):377–386.
Mackay J, Gustafson P, Haddox A, Alpert VM. 2007. The epigenetic and child development in the World Trade Center cohort. Environ Health Perspect 115:1497–1502.
Petersen N, Kolmem M, Hoovey P. 2008. Scaling, Norming, and Equating. Phoenix, AZ: Oryx Press.
Phillips DH, Artz VM. The 32p-postlabeling assay for DNA adducts. Nat Protoc 2(11):2722–2728.
Poller MC, Beland FA. 1992. Integrated biomarkers and measurements and tumor incidence during chronic carcinogenic exposure in animal models: implications for DNA adduct-based human cancer risk assessment. Chem Res Toxicol 5(6):749–755.
Randerath K, Leh J, Hug TK, Randerath E. 1989. Use of the 32p-postlabeling assay to study transplacental carcinogens and transplacental carcinogenesis. IARC Sci Publ 96:189–205.
Rapport MD, Deeney CB, Chung KM, Hustace K. 2001. International behavior problems and scholastic achievement in children: cognitive and behavioral pathways as mediators of outcome. J Clin Child Psychol 30(4):536–551.
Rau VA, Garfinkel R, Perera FP, Andrews H, Barr DB, Whitehead R, et al. 2006. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first three years of life among inner-city children. Pediatrics 118(1):e1845–e1859.
Robinson M, Oddy WH, Li J, Kendall GE, de Klerk NH, Silburn SR, et al. 2008. Pre- and postnatal influences on preschool mental health: a large-scale cohort study. J Child Psychol Psychiatr 49(10):1118–1128.
Rodier PM. 2004. Environmental causes of central nervous system maldevelopment. Pediatrics 113(suppl 3):1078–1083.
Rybacki BA, Rundle A, Saveria AT, Sankey SS, Tang D. 2004. Polycyclic aromatic hydrocarbon-DNA adducts in prostate cancer. Cancer Res 64(24):8854–8859.
Sanson P, Prior S, Smart S. 2008. The impact of early disabilities with and without behaviour problems at 7–8 years: prediction from longitudinal data from infancy to 6 years. J Child Psychol Psychiatr 37(5):529–541.
Saunders CR, Das DK, Ramesh A, Shotlock DC, Mukherjee S. 2008. Benzo[a]pyrene-induced acute necrototoxicity in the F-344 rat: role of oxidative stress. J Appl Toxicol 28(5):427–438.
Stowers SJ, Anderson MW. 1985. Formation and persistence of benzo[a]pyrene metabolite-DNA adducts. Environ Health Perspect 62:313–319.
Swords L, Hennessy E, Heavy C. 2011. Development of the Children’s Attributes About Psychological Problems in their Peers Scale. Child Care Health Dev 37(5):446–455.
Takasawa Y, Takae N, Yoshioka H. 2003. The genotoxicity and carcinogenicity of PAH-DNA adducts is associated with increased levels of PAH-DNA adducts in a case-control study of breast cancer. Breast Cancer Res Treat 75(2):159–166.
Tang D, Li YM, Liu JJ, Chen YH, DU, L Perera FP. 2006. PAH-DNA adducts in cord blood and fetal and child development in a Chinese cohort. Environ Health Perspect 111:1297–1303.
Tang D, Santella RM, Blackwood A, Young TL, Mayer J, Jerrett M, et al. 1999. Aromatic hydrocarbon exposure and childhood control study of lung cancer. Cancer Epidemiol Biomarkers Prev 4(4):341–346.
Viegla F, Matallo G, Vines P. 2003. Bulk DNA adducts and risk
of cancer: a meta-analysis. Cancer Epidemiol Biomarkers Prev 12(2):157–160.
Wacholder S, Chanock S, Garcia-Closas M, El Ghormli L, Rothman N. 2004. Assessing the probability that a positive report is false: an approach for molecular epidemiology studies. J Natl Cancer Inst 96(6):434–442.
Wasserman GA, Liu X, Pine DS, Graziano JH. 2001. Contribution of maternal smoking during pregnancy and lead exposure to early child behavior problems. Neurotoxicol Teratol 23(1):13–21.
Wilson VL, Jones PA. 1983. Inhibition of DNA methylation by chemical carcinogens in vitro. Cell 32(1):239–246.
Wong EF, Gohke J, Griffith WC, Farrow S, Faustman EM. 2004. Assessing the health benefits of air pollution reduction for children. Environ Health Perspect 112:226–232.
Wood JJ. 2006. Effect of anxiety reduction on children’s school performance and social adjustment. Dev Psychol 42(2):345–349.
Wood KA, Youle RJ. 1995. The role of free radicals and p53 in neuron apoptosis in vivo. J Neurosci 15:5851–5857.
World Health Organization. 1986. Principles for evaluating health risks from chemicals during infancy and early childhood: the need for a special approach. In: Environmental Health Criteria 59. Geneva:World Health Organization.
Wongley DD, Chirwa S, Nayyar T, Wu J, Johnson S, Brown LA, et al. 2004a. Inhaled benzo(a)pyrene impairs long-term potentiation in the F1 generation rat dentate gyrus. Cell Mol Biol (Noisy-le-grand) 50(6):715–721.
Wormley DD, Ramesh A, Hood DB. 2004b. Environmental contaminant-mixture effects on CNS development, plasticity, and behavior. Toxicol Appl Pharmacol 197(1):49–65.
Yokota S, Mizuo K, Moriya N, Oshio S, Sugawara I, Takeda K. 2009. Effect of prenatal exposure to diesel exhaust on dopaminergic system in mice. Neurosci Lett 449(1):38–41.