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Prenatal Airborne Polycyclic Aromatic Hydrocarbon Exposure and Child IQ at Age 5 Years

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KEY WORDS
prenatal, fetal, polycyclic aromatic hydrocarbons, air pollution, IQ

ABBREVIATIONS
CI— confidence interval
CCCEH—Columbia Center for Children's Environmental Health
HOME—Home Observation for Measurement of the Environment
PAH—polycyclic aromatic hydrocarbon
WPPSI-R—Wechsler Preschool and Primary Scale of Intelligence-Revised
TONI-3—Test of Maternal Nonverbal Intelligence, Third Edition
ETS— environmental tobacco smoke

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WHAT'S KNOWN ON THIS SUBJECT: Previous studies of the effects of PAHs on neurodevelopment were experimental or assessed mental development at 1, 2, and 3 years of age. Our study indicated that this environmental exposure might have long-term effects.

WHAT THIS STUDY ADDS: This is the first study to report an association between prenatal exposure to PAHs and IQ.

abstract

OBJECTIVE: This study evaluated the relationship between prenatal exposure to airborne polycyclic aromatic hydrocarbons (PAHs) and child intelligence.

METHODS: Children of nonsmoking black or Dominican-American women residing in New York City were monitored from in utero to 5 years of age, with determination of prenatal PAH exposure through personal air monitoring for the mothers during pregnancy. At 5 years of age, intelligence was assessed for 249 children by using the Wechsler Preschool and Primary Scale of Intelligence-Revised. Multivariate linear regression models were used to estimate and to test the associations between prenatal PAH exposure and IQ.

RESULTS: After adjustment for maternal intelligence, quality of the home caretaking environment, environmental tobacco smoke exposure, and other potentially confounding factors, high PAH levels (above the median of 2.26 ng/m^3) were inversely associated with full-scale IQ ($P = .007$) and verbal IQ ($P = .003$) scores. Children in the high-exposure group had full-scale and verbal IQ scores that were 4.31 and 4.67 points lower, respectively, than those of less-exposed children ($\leq$2.26 ng/m^3). The associations between logarithmically transformed, continuous, PAH levels and these IQ measures also were significant (full-scale IQ: $\beta = -3.00$; $P = .009$; verbal IQ: $\beta = -3.53$; $P = .002$).

CONCLUSION: These results provide evidence that environmental PAHs at levels encountered in New York City air can affect children's IQ adversely. *Pediatrics* 2009;124:e195–e202

Polycyclic aromatic hydrocarbons (PAHs) are released to air during incomplete combustion and/or pyrolysis of fossil fuel, tobacco, and other organic material.[1] Although exposure is ubiquitous, urban minority populations represent high-risk groups both for disproportionate exposure to air pollution and for adverse health and developmental outcomes.[2–6] As reported previously, 100% of the mothers in the Columbia Center for Children's Environmental Health (CCCEH) cohort had detectable levels of PAHs in prenatal personal air samples, and 40% reported environmental tobacco smoke (ETS) exposure during pregnancy.[7]

Exposures during the prenatal and early postnatal stages are of particular concern because of the heightened susceptibility of fetuses and infants to diverse environmental pollutants, including PAHs.[8–12] In addition to their more-immediate health effects, certain prenatal exposures may critically affect epigenetic programming and immune, metabolic, and neurologic functions, with consequences manifesting throughout the life span.[13–16] Increased susceptibility during early stages of development is attributed to higher cell proliferation rates, lower immunologic competence, and decreased ability to detoxify chemicals and to repair DNA damage.[8–10] Laboratory experiments have indicated that the fetal brain and nervous system may be particularly sensitive to PAHs.[16–19] For example, in utero exposure to diesel exhaust, which contains a variety of PAHs, was associated with significant reductions in performance on the passive avoidance learning test for both male and female mice and affected the emotional behaviors associated with the serotonergic and dopaminergic systems in the mouse brain.[19] In addition, transplacental exposure of rats to benzo[*a*]pyrene depressed the levels of *N*-methyl-D-aspartate receptor subunit 1 within the hippocampus significantly and, after birth, impaired long-term potentiation, a marker of long-term memory and learning.[20]

A number of PAHs, such as benzo[*a*]pyrene, were shown to be reproductive and developmental toxicants in experimental studies involving prenatal exposure.[17,20,21] In epidemiological studies, transplacental PAH exposure was associated with fetal growth reduction, including reduced birth weight and birth head circumference and/or small size for gestational age, in New York City black, white, and Chinese newborns.[7,22–25] In addition, neurodevelopmental effects have been associated with prenatal exposure to PAHs or with PAH-DNA adducts in cord blood; in the prospective CCCEH cohort study using the Bayley Scales of Infant Development, we found that prenatal exposure to airborne PAHs was associated with reduced Mental Developmental Index scores and increased odds of developmental delay at 3 years of age.[26] Similarly, increased risk of delayed motor development was seen at 2 years of age in a cohort of Chinese children exposed prenatally to PAHs, principally from coal-fired plant emissions, as measured with elevated PAH-DNA adduct levels in cord blood.[27] These significant effects were not seen in a second cohort conceived after the power plant had been shut down.[28] A study in the Czech Republic indicated that schoolchildren in the district of Teplice, which had higher levels of PAHs and other air pollutants from coal-burning than did the comparison district, had a significantly higher rate of teacher referrals for clinical assessment.[29] To date, there have been no reports of associations between PAH exposure and IQ. Here, within the CCCEH cohort study, we examined children's IQ at age 5 in relation to prenatal exposure to PAHs.

METHODS

Sample Selection

A complete description of the cohort and study design is presented elsewhere.[7,26] Briefly, black and Dominican-American women who resided in Washington Heights, Harlem, or the South Bronx in New York, New York, were recruited between 1998 and 2003, through local prenatal care clinics, into a prospective cohort study.[7] To reduce the potential for confounding, the target population was restricted to women who were 18 to 35 years of age, were not cigarette smokers, were not users of other tobacco products or illicit drugs, were free of diabetes mellitus, hypertension, or known HIV infection, and initiated prenatal care by the 20th week of pregnancy. The institutional review board of the New York Presbyterian Medical Center approved the study; informed consent was obtained from all study participants. Of the 392 children and mothers who participated in the cohort study when the child was 5 years of age, 249 English-speaking children were tested with the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) (no Spanish version was available) and had complete information on all explanatory variables. Those children were included in the analyses described below. Table 1 compares characteristics of children and their mothers with complete data ($N = 249$), those with missing covariate or test information ($N = 143$), and those no longer participating in the study at 5 years ($N = 134$). The 3 groups were similar with respect to maternal age, maternal education, home caretaking environment (as measured with the Home Observation for Measurement of the Environment [HOME] inventory, a standard assessment of the quality of

TABLE 1 Characteristics of Children and Mothers When Children Were 5 Years of Age

	Children With Complete Data	Children With Incomplete Data	Children Not Participating at 5 y
Maternal characteristics			
Age, mean ± SD, y	29.7 ± 4.95 (N = 249)	30.7 ± 5.12 (N = 131)	29.6 ± 4.73 (N = 125)
High school education, %	61.8 (N = 249)	65.4 (N = 130)	62.1 (N = 124)
Ethnicity, %[a]			
Black	57.4 (N = 249)	15.3 (N = 131)	28 (N = 125)
Dominican	42.6	84.7	72
HOME score, mean ± SD	40.67 ± 5.63 (N = 249)	38.63 ± 6.20 (N = 112)	37.42 ± 6.13 (N = 14)
TONI-3 score, mean ± SD	21.77 ± 8.60 (N = 249)	19.43 ± 8.59 (N = 114)	18.70 ± 9.07 (N = 20)
PAH level, mean ± SD, ng/m^3	3.48 ± 3.68 (N = 249)	3.54 ± 3.97 (N = 131)	3.85 ± 5.24 (N = 125)
Child characteristics			
Female, %	53.8 (N = 249)	51.9 (N = 131)	45.6 (N = 125)
ETS exposure, %	40.6 (N = 249)	32.5 (N = 126)	36.3 (N = 124)
Gestational age, mean ± SD, wk	39.18 ± 1.52 (N = 216)	39.46 ± 1.25 (N = 108)	39.34 ± 1.58 (N = 95)
Birth length, mean ± SD, cm	50.49 ± 4.19 (N = 239)	51.03 ± 2.50 (N = 124)	50.75 ± 2.28 (N = 114)
Birth weight, mean ± SD, kg[a]	3.36 ± 0.51 (N = 244)	3.47 ± 0.40 (N = 129)	3.33 ± 0.50 (N = 115)
Birth head circumference, mean ± SD, cm	34.11 ± 1.57 (N = 232)	34.38 ± 1.22 (N = 119)	33.99 ± 1.63 (N = 107)
Full-scale IQ, mean ± SD	98.72 ± 13.61 (N = 249)	102.00 ± 14.15 (N = 29)	
Verbal IQ, mean ± SD	93.88 ± 13.79 (N = 249)	97.34 ± 13.76 (N = 29)	
Performance IQ, mean ± SD	104.24 ± 14.44 (N = 249)	106.96 ± 16.57 (N = 29)	

Fully enrolled mothers and children had valid prenatal PAH monitoring, birth outcome, and prenatal questionnaire data. For variables not required for the regression analysis, the numbers of observations varied.

[a] $P \leq .05$ for comparison between children with complete data and children with incomplete data. P values are based on 2-sample t tests for continuous variables and z tests for proportions.

the home environment for children ranging from newborns to adolescents[30]), and maternal intelligence (as measured with the Test of Maternal Nonverbal Intelligence, Third Edition [TONI-3], a language-free measure of general intelligence that is considered to be relatively free of cultural bias[31]).

PAH and ETS Exposure, Newborn Gender, Birth Length, and Birth Weight, and Child IQ Measures

Ethnicity and birth weight differed because of the requirement that children be tested in English; 86 Spanish-speaking, Dominican-American children were excluded from the current sample, which resulted in a larger proportion of black children. This exclusion took place because a comparable version of the WPPSI-R (the neurocognitive outcome measure) in Spanish was not available. Because the birth weight of Dominican-American infants (mean ± SD: 3421 ± 444 g; N = 435) was significantly greater than the birth weight of black infants (mean ± SD: 3274 ± 524 g; N = 235; P = .0003) in this sample, the mean for the total sample (subjects with complete data for all tests) was significantly lower than the mean for subjects with missing data.

Personal Interview

A 45-minute questionnaire was administered by a trained, bilingual interviewer during the last trimester of pregnancy, to obtain demographic, residential, history, health, and environmental data, such as information on active and passive smoking. As in our previous analyses, self-reported exposure to ETS was correlated with cotinine levels measured in the children's cord blood (r = 0.449; $P <$ .0001). The questionnaire also elicited information on dietary PAH exposure (consumption of broiled, fried, grilled, or smoked meat) and socioeconomic information related to income and education.[7] Postnatal interviews were administered in person at 6 months and annually thereafter, to determine any changes in residence, exposure to ETS, or other health or environmental conditions.

Prenatal Personal PAH Assessment

During the third trimester of pregnancy, personal monitoring was conducted as described previously.[7] Seasonal variation in air pollution is relatively minor in New York City, and there is constant, chronic exposure to air pollution, largely from transportation sources. Therefore, as in previous studies with this cohort,[26] a single time point for prenatal personal air monitoring was considered a reasonable indicator of chronic prenatal exposure through inhalation during the prenatal exposure period. We did not consider using ambient monitoring data because they are not available for PAHs in New York City. Vapors and particles of ≤2.5 μg in diameter were collected with precleaned quartz microfiber filters and precleaned polyurethane foam cartridges. The samples were analyzed at Southwest Research Institute for benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, disbenz[*a,h*]anthracene, and benzo[*g,h,i*]perylene. For quality

control, each personal monitoring result was assessed with respect to accuracy in flow rate, time, and completeness of documentation. In support of the use of personal monitoring to assess indoor and outdoor exposure, a parallel study using the same approach to monitor the personal air of pregnant women in Krakow, Poland, showed that, for a subset of the cohort with simultaneous monitoring of personal, indoor, and outdoor PAH levels, the 3 measurements were highly correlated (pairwise Spearman coefficients of $\geq$0.84; $P < .01$).[32]

Outcomes

An experienced research worker, trained to reliability by Dr Jeffrey Jankowski (Albert Einstein College of Medicine, Bronx, NY), administered the WPPSI-R, an intelligence test designed for children 2.5 years to 7.25 years of age. The research worker was blinded to each child's level of exposure. The WPPSI-R provides verbal, performance, and full-scale IQ scores. Scores have a mean of 100 and a SD of 15. Scores of <70 are classified as extremely low, 70 to 79 as borderline, 80 to 89 as low average, 90 to 109 as average, 110 to 119 as high average, 120 to 129 as superior, and $\geq$130 as very superior.

Statistical Analyses

The sample ($N = 249$) in the present analyses included the participants with valid personal air monitoring data, complete questionnaire data on covariates of interest, and valid data on IQ at age 5. In some cases, covariate or test information was missing as a result of loss to follow-up monitoring or lack of a biological specimen for biomarker analysis. We also excluded children who were not tested in English. This exclusion took place because a comparable version of the WPPSI-R in Spanish was not available.

As in previous analyses,[7,24,26] a composite PAH variable was computed from 8 carcinogenic PAH air concentration measurements; these 8 measurements were all correlated significantly (r values of 0.34–0.94 and all P values of <.001 in Spearman rank-order correlation analyses). This variable was dichotomized at the median for the population (2.26 ng/m^3) to obtain a measure of high/low exposure. In separate analyses, PAH levels were logarithmically transformed and treated as a continuous variable. PAH levels were logarithmically transformed to reduce skewness and to stabilize variance. Covariates were treated as follows: ETS exposure as a dichotomous variable (presence or absence of smokers in the household during pregnancy and after delivery), concentrations of lead measured in cord blood as a continuous variable, concentrations of cotinine in cord blood (as a measure of active maternal smoking) as a dichotomous variable (>25 ng/mL), and concentrations of chlorpyrifos in cord blood as a dichotomous variable (6.17 pg/g), as described previously.[33]

Correlations between continuous airborne PAH levels and ETS exposure ($r = 0.118$; $P = .002$) and dietary PAH levels ($r = -0.036$; $P = .35$) were examined by using Spearman rank-order correlation. Multivariate regression was used to examine the associations between prenatal PAH exposure and child IQ at age 5. Independent risk factors and potential confounders were identified from the literature or from our previous studies and were retained in the final models if they were associated with IQ at $P < .1$. Prenatal exposure to lead (mean $\pm$ SD: 1.06 $\pm$ 0.74 μg/dL), maternal active smoking (measured as cotinine levels), and chlorpyrifos levels were not significant predictors of IQ in this sample (all $P >$ .1); therefore, these covariates were not included in the final model. Final covariates included in the model for child intelligence included ETS exposure during pregnancy, child's gender, child's gestational age, ethnicity, mother's intelligence (measured with the TONI-3), mother's completed years of education by child age of 5 years, and quality of the early home caretaking environment (measured with the HOME inventory) at 3 years of age. Gestational age was based on medical record data for almost all subjects. Where those data were missing, gestational age was calculated from the date of the last menstrual period. Ethnic differences were tested by including an interaction term (PAH $\times$ ethnicity) in the model. Possible mediation of the effects on IQ through PAH-related reductions in fetal head circumference was tested by including birth head circumference in the model. All effect estimates, 95% confidence intervals (CIs), and P values (α set at .05) were generated by using SAS 9.1.0.3 (SAS Institute, Cary, NC).

RESULTS

Among the 249 children 5 years of age, prenatal PAH exposure levels ranged from 0.49 ng/m^3 to 34.48 ng/m^3. A total of 140 (56.2%) of the 249 children were classified as having high PAH exposure (>2.26 ng/m^3), with 2.26 ng/m^3 being the median for the entire cohort. The mean $\pm$ SD full-scale IQ score at 5 years of age was 98.72 $\pm$ 13.61 (range: 61–141). Full-scale IQ scores at 5 years of age were correlated with maternal IQ scores ($r = 0.27$; $P < .0001$). Table 2 shows the characteristics of the 249 children included in the analysis, stratified according to PAH exposure. In 2-sample z tests for proportions, there were significant differences between high- and low-exposure groups in the distributions of maternal high school degree and infant's verbal IQ and full-scale IQ but not performance IQ (Table 2). In univariate regression analyses, women who had higher levels of exposure to PAHs during pregnancy

TABLE 2 Demographic Characteristics of Sample Included in Analyses, According to Prenatal PAH Exposure Level ($N = 249$)

	High PAH Exposure ($N = 140$)	Low PAH Exposure ($N = 109$)	P[a]
Maternal characteristics			
ETS exposure, %	45.0	34.8	NS
Age, mean ± SD, y	29.4 ± 4.81	30.0 ± 5.14	NS
High school education, %	56.4	68.8	.046
Ethnicity, %			NS
Black	57.9	56.9	
Dominican	42.1	43.1	
HOME score, mean ± SD	40.1 ± 5.6	41.4 ± 5.6	NS
TONI-3 score, mean ± SD	21.7 ± 8.0	21.9 ± 9.4	NS
Child characteristics			
Female, %	55.7	51.4	NS
Gestational age, mean ± SD, wk	39.2 ± 1.42 ($N = 121$)	39.2 ± 1.66 ($N = 95$)	NS
Birth length, mean ± SD, cm	50.5 ± 3.01 ($N = 137$)	50.5 ± 5.41 ($N = 102$)	NS
Birth weight, mean ± SD, kg	3.33 ± 0.52 ($N = 138$)	3.40 ± 0.49 ($N = 106$)	NS
Birth head circumference, mean ± SD, cm	34.0 ± 1.62 ($N = 134$)	34.3 ± 1.50 ($N = 98$)	NS
Full-scale IQ, mean ± SD	96.5 ± 13.1	101.6 ± 13.7	.003
Verbal IQ, mean ± SD	91.5 ± 12.8	96.9 ± 14.5	.002
Performance IQ, mean ± SD	102.9 ± 15	105.9 ± 13.6	NS

High PAH exposure indicates >2.26 ng/m^3; low exposure, ≤2.26 ng/m^3; NS, not significant.

[a] P values are based on 2-sample t tests for continuous variables and z tests for proportions.

were significantly more likely to have infants with lower full-scale and verbal IQ scores tested at age 5; the deficits in IQ scores were 5.4 points (95% CI: 1.95–8.85; $P = .003$) and 5.1 points (95% CI: 1.73–8.47; $P = .002$), respectively. As shown in Table 3, the inverse associations between high/low PAH exposure and full-scale and verbal IQ scores remained significant after adjustment for covariates (full-scale IQ: $\beta = -4.31$ [95% CI: −7.41 to −1.21]; $P = .007$; verbal IQ: $\beta = -4.67$ [95% CI: −7.73 to −1.61]; $P = .003$). The association with performance IQ was inverse but not significant ($\beta = -2.37$ [95% CI: −5.75 to 1.01]; $P = .17$) (Fig 1). The associations between logarithmically transformed, continuous, PAH levels as the independent variable and IQ also were significant for full-scale IQ ($\beta = -3.00$ [95% CI: −5.24 to −0.77]; $P = .009$) and verbal IQ ($\beta = -3.53$ [95% CI: −5.73 to −1.33]; $P = .002$). For performance IQ, the association was inverse but not significant ($\beta = -1.47$ [95% CI: −3.91 to 0.96]; $P = .24$). Controlling for postnatal exposure to ETS did not influence the results.

There were no significant ethnic differences in the relationship between PAH levels and IQ scores (full-scale IQ: $P = .36$; verbal IQ: $P = .62$; performance IQ: $P = .35$). Birth head circumference was neither a significant predictor of IQ nor a mediator of the observed PAH effect on IQ. Air monitoring data were not available to control directly for postnatal PAH exposure; however, controlling for changes in residence by age 3, as a proxy for variations in PAH exposure between the prenatal and postnatal periods, the inverse associations between prenatal PAH levels and IQ remained significant (dichotomous PAH levels: full-scale IQ: $\beta = -4.27$; $P = .007$; verbal IQ: $\beta = -4.65$; $P = .003$; logarithmically transformed PAH levels: full-scale IQ: $\beta = -2.94$; $P = .01$; verbal IQ: $\beta = -3.5$; $P = .002$).

TABLE 3 Associations Between Prenatal PAH Exposure and Children's Full- Scale IQ, Verbal IQ, and Performance IQ

	Full-Scale IQ ($N = 249$)		Verbal IQ ($N = 249$)		Performance IQ ($N = 249$)	
	β	P	β	P	β	P
PAH exposure (high/low)	−4.307	.007	−4.668	.003	−2.369	.170
ETS exposure	1.736	.289	1.803	.265	1.609	.368
Gender	3.632	.021	4.695	.002	2.354	.168
Maternal education	5.233	.002	4.510	.007	4.969	.007
Ethnicity	1.440	.373	6.174	.000	−4.761	.007
HOME score	0.332	.025	0.468	.001	0.121	.453
TONI-3 score	0.305	.001	0.147	.114	0.422	<.0001

Variables are as defined in Table 2. Intercepts were as follows: full-scale IQ, 74.294 ($P < .0001$); verbal IQ, 64.658 ($P < .0001$); performance IQ, 64.658 ($P < .0001$).

DISCUSSION

As discussed above, previous results from this cohort indicated that exposure to PAH air pollutants in New York City during pregnancy is a risk factor for developmental delay at age 3, as identified with the Bayley Scales of Infant Development.[26] The present analysis suggests continued effects of prenatal PAH exposure on child IQ at age 5. After adjustment for potential confounders, full-scale and verbal IQ scores of the high- and low-exposure groups differed by 4.31 points and 4.67 points, respectively. The observed decrease in full-scale IQ was similar to that reported for children with lifetime average blood lead concentrations between 5 and 9.9 μg/dL, compared with children with lifetime average blood lead concentrations of <5 μg/dL (difference of −4.9 IQ points).[34] The present findings are of concern because verbal and full-scale IQ scores measured with the WPPSI-R during the preschool period were shown to be predictive of subsequent elementary school performance in a range of populations.[35–38] The children are being monitored to 11 years of age, and subsequent testing should provide a picture of the longer-term developmental outcomes of children in the cohort.

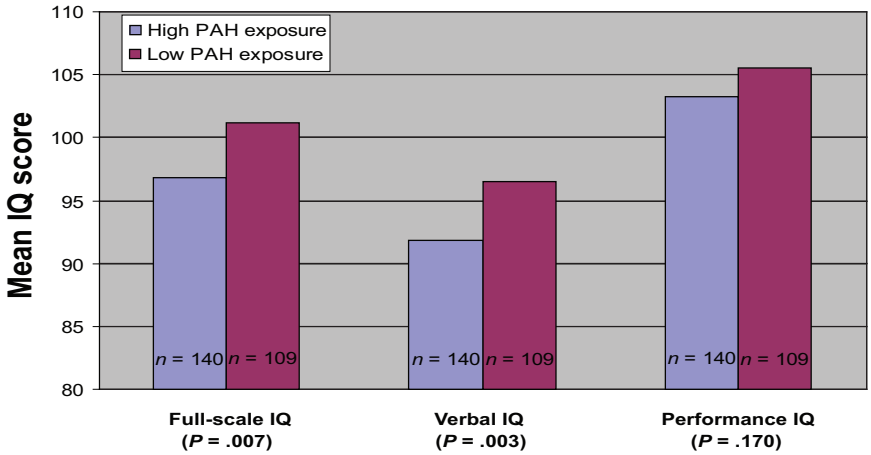

FIGURE 1

Differences in full-scale, verbal, and performance IQ scores associated with high levels of prenatal PAH exposure ($N = 249$). Mean IQ scores were adjusted for ETS exposure during pregnancy, child's gender, ethnicity, mother's intelligence (TONI-3), mother's education, and quality of the home caretaking environment (HOME inventory).

To our knowledge, there have been no previous epidemiological studies of the effects of prenatal PAH exposure on child IQ. However, the findings are consistent with previous research (reviewed above) indicating that fetal exposure to PAHs can affect the neurodevelopment of children. The mechanisms through which PAHs may affect the developing brain are not fully known. Fetal toxicity may be caused by endocrine disruption,[19,21,39] binding to placental growth factor receptors resulting in decreased exchange of oxygen and nutrients,[23] binding to the human Ah receptor to induce cytochrome P450 enzymes,[40] DNA damage resulting in activation of apoptotic pathways,[41–43] epigenetic effects,[44] or oxidative stress attributable to inhibition of the brain antioxidant-scavenging system.[45]

We accounted for factors other than PAH exposures that are known to affect intellectual development, including the quality of the proximal caretaking environment, which was not a significant predictor in our model (Table 3), and we assessed intelligence at an age when IQ can be measured reliably. This study has the additional advantage of being based on individual prenatal exposure data from personal monitoring, biomarker data on lead and cotinine levels, and extensive medical record and questionnaire data. However, relationships observed for low-income, minority women might be different from those for women of other races or ethnic, cultural, or socioeconomic backgrounds. We also lacked postnatal monitoring data and controlled indirectly for postnatal PAH exposure. However, humans pass more biological milestones before birth than at any other time in their lives,[46] and the prenatal period is highly sensitive to neurotoxic effects of environmental contaminants.[47] Additional studies are needed to distinguish the effects of prenatal and postnatal exposure to PAHs and to confirm the present findings.

CONCLUSIONS

This study provides evidence that environmental PAHs at levels encountered in the air of New York City can affect child IQ scores adversely. The results require confirmation but are of potential concern, because IQ is an important predictor of subsequent academic performance.[36] PAHs are widespread in urban environments throughout the world, largely as a result of fossil fuel combustion. Fortunately, airborne PAH concentrations can be reduced through currently available pollution controls, greater energy efficiency, use of alternative energy sources,[48] and regulatory intervention to remove polluting sources.[49]

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