Effects of prenatal polycyclic aromatic hydrocarbon exposure and environmental tobacco smoke on child IQ in a Chinese cohort

F. Perera, T.Y. Li, C. Lin, D. Tang

Abstract

Objective: This study of a birth cohort in the city of Tongliang in Chongqing, China, evaluated the relationship between two prenatal exposures (polycyclic aromatic hydrocarbons (PAH) and environmental tobacco smoke (ETS)) and child intelligence quotient (IQ) as measured by the Wechsler Preschool and Primary Scale of Intelligence at age 5. A coal-fired power plant was the major source of ambient PAH in this city. We tested the hypothesis that, after adjusting for potential confounders, prenatal exposure to these pollutants would be associated with lower IQ scores at 5 years of age.

Methods: Nonsmoking mothers and children were enrolled before delivery. PAH exposure was measured by DNA adducts in umbilical cord white blood cells using High-Performance Liquid Chromatography-Fluorescence. Estimated exposure to environmental tobacco smoke was based on personal interview. At age 5 years, scores for verbal, performance, and full scale IQ were obtained. Multiple regression was used to test the main effects of adducts and environmental tobacco smoke on IQ and to explore the interactions between these exposures on IQ. Results: After adjusting for potential confounders, neither DNA adducts nor exposure to environmental tobacco smoke had significant main effects on IQ. However, significant interactions between adducts and environmental tobacco smoke were observed on full scale (p = 0.025) and verbal (p = 0.029) IQ scores, indicating that the adverse effects of prenatal PAH exposure became greater as exposure to environmental tobacco smoke increased. The interaction on performance IQ score was not significant (p = 0.135).

Conclusion: These results suggest that exposure of pregnant women to emissions of PAHs from the coal-burning plant, in combination with prenatal exposure to environmental tobacco smoke, may have adversely affected cognitive function of children at age 5. The polluting coal-fired plant has since been closed by the government, with likely important benefits to child health and development.

1. Introduction

Molecular and epidemiologic research has shown that fetuses, infants, and young children are more susceptible than adults to the harmful effects of a variety of environmental contaminants including polycyclic aromatic hydrocarbons (PAH), lead, and environmental tobacco smoke (ETS) (ATSDR, 2005; National Research Council, 1993; Perera et al., 2005a; World Health Organization, 1986). Polycyclic aromatic hydrocarbons are toxic, mutagenic, and carcinoogenic air pollutants that are generated by the incomplete combustion of fossil fuels such as coal, diesel, and gasoline (Bostrom et al., 2002); they are also present in tobacco smoke and grilled or broiled foods. PAH-DNA adduct concentrations in both maternal and cord blood have been shown to increase with increasing ambient exposure to PAH, although there is substantial interindividual variation in adduct formation (Perera et al., 2005a; Whyatt et al., 1998). Because PAH-DNA adducts reflect individual variation in exposure, absorption, metabolic activation, and DNA repair, they provide an informative biologic dosimeter that has been associated with risk of cancer (Bartsch et al., 1983; Pelkonen et al., 1980; Tang et al., 2001) and more recently with neurodevelopmental effects (Perera et al., 2007; Tang et al., 2006).

Experimental animal studies have demonstrated that benzo(a)pyrene (BaP), a representative PAH, is a reproductive
toxicant (Archibong et al., 2002) and produces a variety of neurodevelopmental effects including impairment of memory and ability to learn, consistent with observed alterations in the expression of key genes involved in long-term potentiation (Saunders et al., 2002, 2003; Wormley et al., 2004). In epidemiologic studies, prenatal exposure to PAH has been associated with reduced birth weight, length, and head circumference (Choi et al., 2006; Perera et al., 2003, 1998; Sram et al., 2005). In the present Chinese cohort, reduction of head circumference was associated with PAH-DNA adducts in cord blood (Tang et al., 2006). Several studies have associated prenatal PAH exposure with decrements in cognitive function. For example, children born during the years of maximal air pollution in the Czech Republic had learning disorders that were attributed in part to elevated levels of PAH in the atmosphere from the mining and combustion of coal (Otto et al., 1997). Children in New York City who were more highly exposed to PAH in utero had significantly decreased Bayley Mental Development Index (MDI) scores, were more likely to be developmentally delayed at 3 years of age (Perera et al., 2006), and had reduced IQ scores measured at the age of 5 (Perera et al., 2009). In the present China cohort, higher PAH-DNA adducts in cord blood were associated with decreased scores on the Gesell Test at age 2 (Perera et al., 2008; Tang et al., 2008). In a second cohort of children conceived after the Tongliang coal-fired power plant was closed, this association was no longer observed, indicating direct benefits of this intervention (Perera et al., 2008).

Prenatal ETS exposure is a known risk factor for neurodevelopmental impairment (Rauh et al., 2006). Our previous studies in New York City found a significant interaction between PAH-DNA adducts in cord blood and prenatal ETS exposure on birth weight (Perera et al., 2005b) and on 3 year mental development (Perera et al., 2006). We have therefore explored both main effects and interactions between these pollutants and child IQ in the Tongliang cohort.

2. Materials and methods

2.1. Study population

The present cohort study was conducted in Tongliang, Chongqing, which has a population of around 100,000 and is situated in a basin approximately 3 km in diameter. Before its permanent shutdown in December 2004, a coal-fired power plant located south of the town center operated every year from 1 December to 31 May to compensate for the insufficient hydraulic power during the dry season (Chow et al., 2006; Tang et al., 2006). The plant was not equipped with modern pollution reduction technology and combusted about 25,000 tons of coal during each 6-month period of operation. This report concerns the cohort of children whose gestational period included the months of power plant operation from 1 December, 2001 to 31 May, 2002.

The main exposure of interest (PAH) resulted primarily from the burning of coal fuel by the local power plant. In 1995 nearly all domestic heating and cooking units were converted to natural gas and in 2002 motor vehicles were limited in number. Air monitoring analyses carried out as part of the study showed that PAH of medium molecular weight (168–266 Da) increased by 1.5–3.5 times during the Tongliang power plant's operational period (Chow et al., 2006).

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2.2. Study subjects

Subjects were children born to nonsmoking Chinese women who gave birth at any one of three Tongliang county hospitals between 4 March, 2002 and 19 June, 2002. The women were selected using a screening questionnaire when they checked in for delivery. Eligibility criteria included non-smoking status, age ≥ 20 years, and residence within 2.5 km of the Tongliang power plant. Of 150 eligible consenting women, 149 were enrolled, completed the interview, and contributed a cord blood sample at the time of delivery; 131 had cord adduct data. One hundred twenty two mother–child pairs remained in the study 5 years after the study had begun (82% retention rate). We measured IQ in the 5-year old using the Shanghai version of the Wechsler Preschool and Primary Scale of Intelligence. One hundred children had complete data on all measures and variables required for the analysis. Tests were not completed on 28 children because the families either had moved or could not be scheduled for testing. All subjects signed the consent form approved by the Columbia University Institutional Review Board and Chongqing University of Medical Sciences, and testing was completed in one session.

2.3. Personal interview

A trained interviewer administered a 45 min questionnaire after delivery that elicited demographic information, lifetime residential history (location of birth and duration of each residency), history of active and passive smoking, occupational exposure during pregnancy (chemical exposure, including coal products from hot asphalt or tar roofing material, agriculture herbicides, and insecticides), and consumption of PAH-containing meat during pregnancy (frequency of eating broiled or red meat/meat products). ETS exposure was measured by a set of questions about timing, frequency, and the amount of exposure to cigarette, cigar, and pipe smoke in the home. Socioeconomic information related to income and education was also collected. As reported in previous studies, the Chinese are reluctant to reveal their true income (Xu et al., 2006); hence, we considered education level a more reliable indicator of socioeconomic status. Few women reported occupational exposure to chemicals.

2.4. Biological sample collection and analysis

Umbilical cord blood was collected at delivery. The blood samples for PAH-DNA adducts were collected in heparinized BD Vacutainer tubes (10 mL, green) (Becton Dickinson, Franklin Lakes, NJ, USA). The blood samples for lead analysis were collected in EDTA Vacutainer tubes (4 mL, lavender). Samples were transported to the field laboratory at the Tongliang County Hospital immediately after collection.

The buffy coat, packed red blood cells, and plasma were separated and stored at −70 °C. As a proxy for PAH-DNA adducts, BaP-DNA adducts were analyzed in extracted white blood cell DNA using a high-performance liquid chromatography (HPLC)/fluorescence method that detects BaP tetraols (Alexandrov et al., 1992; Rojas et al., 1994); the method has been modified as described previously (Tang et al., 2006). Briefly, 100 μg of DNA was used for each analysis. Many precautions were taken to avoid the presence of fluorescent contaminants. We calculated tetraol concentrations by comparing the samples analyzed with an external calibration curve generated from the fluorescence peak of a known amount of authentic benzo[a]-pyrene diol epoxide (BPDE) tetraol standard each time a set of samples was analyzed. The correlation coefficient was 0.98, and the mean coefficient of variation for analyses repeated on different days was 12%. The detection threshold of BPDE tetraols [r-7,c-10,t-8,t-9-tetrahydroxy-7,8,9,10-tetrahydrobenzo(a)pyrene (BaP tetraol I-2)] and [r-7,c-10,t-8-tetrahydroxy-7,8,9,10-tetrahydrobenzo(a)pyrene (BaP tetraol I-1)] was 0.25 adducts per 10⁸ nucleotides (signal-to-noise ratio ≥ 3) so that, in the present study, with 100 μg DNA, this assay could detect 0.25 adducts per 10⁸ nucleotides. As in prior studies, nondetectable samples were assigned a value of 0.25/2 = 0.125 per 10⁸ nucleotides. Assays were performed on all samples that were of adequate quantity and quality for analysis. All samples were run coded. Lead is a known neurotoxicant, released from coal combustion and from leaded gasoline (ATSDR, 2005; Canfield et al., 2003; Guo et al., 2002). In order to control for possible confounding from lead exposure, we sent portions of umbilical cord blood to the Laboratory of the Department of Occupational Health, School of Public Health, Fudan University in Shanghai, China. As previously described (Tang et al., 2008), whole blood samples were analyzed using the standard U.S. Environmental Protection Agency (EPA) method, the PE-800 Zeeman atomic absorption spectrometer with Zeeman background correction system (U.S. Environmental Protection Agency, 2007).

2.5. Outcomes

The Wechsler Preschool and Primary Scale of Intelligence is a standardized Intelligence Quotient (IQ) test designed for children 2 years and 6 months to 7 years and 3 months of age. The Shanghai version of the Wechsler Preschool and Primary Scale of Intelligence (1985) which was standardized against a Shanghai population was administered at age 5. The instrument has been widely used in China (Guoian et al., 1996). The test has three main scales: a verbal scale, which measures acquired knowledge verbal reasoning and comprehension, and attention to verbal stimuli; a performance scale, which measures fluid reasoning, spatial processing, attentiveness to detail, and visual–motor integration; and a full scale which measures general intellectual functions. Raw scores were converted to corresponding IQ scores and age equivalents and percentile ranks were estimated using standardized norms. Each child was assigned an intelligence quotient in each of the three scales. The mean of the standardized IQ is 100 with a standard deviation (SD) of 15. Scores of < 70 are classified as extremely low, 70–79 as borderline, 80–89 as low average, 90–109 as average, 110–119 as high average, 120–129 as superior, and ≥ 130 as very superior.

Testing was conducted by trained physicians to maximize reliable assessment and valid interpretation. Testers completed a 1-year course at Shanghai Jiaotong University and passed standardized exams to become certified. Therefore, both inter-examiner and intra-examiner variability were minimal.
Further, the two examiners split the testing by domains, not by subjects. As a result, for any one domain, all subjects were tested by the same examiner. Testing was completed in one session.

After delivery, research workers abstracted relevant information from maternal and infant medical records on covariates including date of delivery, gestational age, and sex of newborn. Other covariates were derived from questionnaire data on socioeconomic status and environmental exposures.

2.6. Statistical methods

The purpose of the statistical analysis was to assess the separate and combined effects of PAH-DNA adduct levels and prenatal ETS on the age-adjusted full scale, verbal and performance IQ scores using linear regression models. Adduct levels were natural (ln) log transformed to normalize the distribution and stabilize the variance. As in previous studies, adducts were also dichotomized as (a) detectable vs. non-detectable and (b) above and below the median of detectable adducts. The cutpoint for detectable adducts was 0.25 per 10^8 nucleotides. The median of detectable adducts was 0.356 per 10^8 nucleotides. We used two measures of ETS exposure— one was the hours of exposure per day, analyzed as a continuous variable. The other measure was a dichotomous variable of the presence or absence of smokers at the mother's workplace or home. We used these measures because women were able to estimate these variables more reliably than the actual amount smoked by others or the timing of those exposures. IQ test scores were analyzed in the original continuous scale.

Subjects who had complete data on IQ test scores, cord adducts, prenatal ETS, and major covariates of interest were included (n = 100). This group was compared with respect to major demographic and exposure characteristics to the group of subjects who were excluded due to missing data (n = 49) (Table 1). Two-sample t-test was used to compare the two groups with respect to mother's age, gestational age, and all IQ scores. Nonparametric Mann–Whitney test was used to compare other continuous variables because of their distributional properties. All categorical variables were analyzed using the chi-squared test.

The main effects of PAH-DNA adduct levels and prenatal ETS on IQ test scores were analyzed by simple linear regression, followed by multiple linear regression. Based on the literature and our prior studies we included cord lead (log transformed), gestational age, mother's age, gender of the child, and maternal education (< high school; ≥ high school) as known or potential risk factors. Dietary PAH was evaluated as a source of PAH and potential confounder. However, among the 100 mothers–child pairs included in the analysis, 90 mothers reported no intake of broiled, barbecued, or charred meat, poultry or fish during pregnancy. The other 10 mothers did not frequently consume these foods during pregnancy. There was no correlation between dietary PAH and cord adducts (Spearman's rho between the dietary PAH index and cord adduct level for the 100 pairs, r = 0.080).

As in previous studies (Pereira et al., 2004, 2006, 2007), the combined effects of PAH-DNA adducts and prenatal ETS exposure were analyzed by including an interaction term (adduct*ETS). Adduct*lead interactions were also explored.

3. Results

Of the 149 mother–child pairs enrolled, 131 had cord adduct data, and 122 children completed the Wechsler IQ test at 5 year follow-up. One hundred pairs had complete data on all variables required for modeling including cord adducts, IQ test scores, prenatal ETS exposure data, mother's education, gestational age, and cord lead. There was no significant difference between the inclusion and exclusion groups in any of the cord adduct measures (see Table 1). The inclusion and exclusion groups were comparable in all other demographic and exposure characteristics shown in Table 1 except for maternal education. The inclusion group had a significantly higher percentage of mothers with high school or higher education (60%) as compared to the excluded group (34%).

The Spearman's correlation coefficients between cord adduct levels and prenatal ETS were not significant, regardless of which measures of cord adducts and ETS were used: e.g., for cord adducts in the original scale and prenatal ETS as continuous variables (r = 0.083, 95% CI = (−0.108, 0.284), N = 100) and for cord adducts as detectable/non-detectable and prenatal ETS dichotomized (r = −0.070, 95% CI = (−0.245, 0.145), N = 100). All three IQ test scores were significantly intercorrelated at p < 0.001. Pearson's correlation coefficients were 0.853 between the full scale and verbal scores, 0.698 between the full scale and performance scores, and 0.484 between the verbal and performance scores. We did not find log-transformed cord lead to be associated with full scale IQ. In simple linear regression the regression coefficients (beta), representing the change in IQ score per one unit increase in log-transformed cord lead, were all non significant: full scale IQ beta = (−2.51, 95% CI = (−9.48, 4.46), p-value = 0.476); verbal IQ (beta = −0.52, 95% CI = (−7.73, 6.68), p-value = 0.886); performance IQ (beta = −4.28, 95% CI = (−11.84, 3.28), p-value = 0.264).

Both PAH-DNA adducts and prenatal ETS were generally inversely, but not significantly, associated with the IQ test scores in the multiple linear regression models (see Table 2(a)). After adjusting for potential confounders, neither PAH-DNA adducts nor ETS had significant main effects on child IQ. However, as shown in Table 2(b), significant interactions were observed between log transformed cord adducts and prenatal ETS (hour/day) on IQ scores, after adjusting for confounders. Specifically, a one hour/day increase in ETS would be expected to result in a significant −10.10 point/(ln) cord adduct (95% CI = (−18.90, −1.29, p = 0.025) change in the slope of the linear relationship between full scale IQ and (ln) cord adduct; a −10.35 point/(ln) cord adduct (95% CI = (−19.61, −1.10, p = 0.029) change in the slope of verbal IQ and (ln) cord adduct; and a nonsignificant −7.78 point/(ln) cord adduct change in the slope of performance IQ/(ln) cord adduct. Negative interactions indicate that

### Table 1
Demographic and exposure characteristics of the study sample.

<table>
<thead>
<tr>
<th></th>
<th>Subjects included in the analysis (N=100)</th>
<th>Subjects excluded</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD or count (%)</td>
<td>Mean ± SD or count (%)</td>
<td></td>
</tr>
<tr>
<td>Mother's age, years</td>
<td>25.12 ± 3.14</td>
<td>25.59 ± 3.40</td>
<td>48</td>
</tr>
<tr>
<td>Maternal age, % ≥ high school</td>
<td>60 (60.0%)</td>
<td>17 (34.7%)</td>
<td>49</td>
</tr>
<tr>
<td>Gestational age, days</td>
<td>277.72 ± 10.22</td>
<td>277.94 ± 12.89</td>
<td>32</td>
</tr>
<tr>
<td>Gender, % female</td>
<td>49 (49.0%)</td>
<td>25 (51.0%)</td>
<td>49</td>
</tr>
<tr>
<td>Cord adduct level (per 10^-8 nucleotides)</td>
<td>0.32 ± 0.14</td>
<td>0.33 ± 0.13</td>
<td>31</td>
</tr>
<tr>
<td>Cord adduct, % detectable</td>
<td>79 (79.0%)</td>
<td>25 (50.6%)</td>
<td>31</td>
</tr>
<tr>
<td>Cord adduct, % above median of detectable</td>
<td>37 (37.0%)</td>
<td>15 (48.4%)</td>
<td>31</td>
</tr>
<tr>
<td>Cord lead level, (µg/L)</td>
<td>3.58 ± 1.55</td>
<td>4.30 ± 2.30</td>
<td>49</td>
</tr>
<tr>
<td>Prenatal ETS, (hour/day)</td>
<td>0.32 ± 0.61</td>
<td>0.52 ± 1.76</td>
<td>49</td>
</tr>
<tr>
<td>Prenatal ETS, % with smokers at work or home</td>
<td>70 (70%)</td>
<td>26 (54.2%)</td>
<td>48</td>
</tr>
<tr>
<td>Full scale IQ, mean score</td>
<td>98.38 ± 14.69</td>
<td>101.23 ± 13.60</td>
<td>22</td>
</tr>
<tr>
<td>Verbal IQ, mean score</td>
<td>97.38 ± 15.15</td>
<td>100.36 ± 12.74</td>
<td>22</td>
</tr>
<tr>
<td>Performance IQ, mean score</td>
<td>99.67 ± 16.00</td>
<td>102.05 ± 17.08</td>
<td>22</td>
</tr>
</tbody>
</table>

* The inclusion criteria were: availability of complete data on IQ, cord adducts, prenatal ETS (hour/day), cord lead, maternal education, and gestational age.

<sup>a</sup> Maternal education was dichotomized as equal to or higher than high school vs. lower than high school.

<sup>b</sup> Significant difference (p < 0.05) between the inclusion and exclusion groups.

<sup>c</sup> Cord adducts were dichotomized at the median of detectable (0.356 per 10^-8 nucleotides).

<sup>d</sup> Prenatal ETS was defined as whether or not there were smokers at work or home during pregnancy.
the adverse effects of cord adducts on IQ become greater as ETS increases.

Based on the interaction models, the effects of adducts within three groups of ETS exposure (0, 0.5, 1 hour/day) were estimated and are plotted in Fig. 1 (a–c). (See figures for details). The figures show the estimated change in the relationship between cord adducts and IQ at varying levels of ETS exposure, illustrating that the relationship becomes increasingly inverse with greater co-exposure to ETS. The slopes in the figures represent the effect of a one (ln) unit increase of cord adducts on IQ. For those mothers exposed to ETS for one hour/day we estimate that a one (ln) unit increase in cord adduct level corresponded to a 9.37 point reduction in the full scale IQ test score and a 8.92 point reduction in the verbal IQ test score as compared to a 4.32 and 3.74 point reduction, respectively, for those mothers exposed to ETS for only 0.5 hour/day.

Significant interactions were also observed between cord adducts dichotomized as detectable and non-detectable and prenatal ETS (hour/day) on IQ scores. Among children with detectable cord blood PAH-DNA adducts, a one hour/day increase in prenatal ETS corresponded to an estimated 10.07 (95%CI=[17.29, 2.85], p=0.007) point average decrease in the full scale IQ, a 8.81 (95%CI=[16.43, 1.19], p=0.024) point average decrease in verbal IQ, and a 9.79 (95%CI=[18.19, 1.39], p=0.023) point average decrease in performance IQ. In contrast, among those with non-detectable cord blood PAH-DNA adducts, IQ test scores did not change significantly as prenatal ETS exposure (hour/day) increased. The difference in the effect of a one hour/day increase in prenatal ETS exposure was calculated for the two cord adduct groups: the group with adduct levels above the median of detectable adducts and the group below the median of detectable (the reference group). The difference in effect was −11.83 points for full scale IQ (95%CI=[−20.69, −2.98], p=0.009), −10.39 points for the verbal scale (95%CI=[−19.73, −1.05], p=0.030) and −10.90 points for the performance scale (95%CI=[−21.19, −0.61], p=0.038) (see Table 2(b)). Children who were exposed to cigarette smoke during pregnancy and had detectable cord adducts were less likely to have above average IQ test scores and were more likely to have below average scores compared to children who were unexposed to cigarette smoke and had non-detectable cord adducts (see Table 3).

The interactions between dichotomized prenatal ETS exposure (modeled as presence or absence of smokers at work or home during pregnancy) and the continuous or dichotomous measures of cord adducts on IQ test scores were generally negative (adverse) as we hypothesized. However, only the interaction on verbal IQ between prenatal ETS and cord adducts (above and below the median value for detectable adducts) reached borderline significance. For those children with a cord adduct level below the median of detectable adducts, co-exposure to ETS resulted in a 4.43 (95%CI=[−2.26, 11.13], p=0.244) point increase in verbal IQ. However, for those children with cord adduct levels above the median of detectable adducts, co-exposure to ETS resulted in a 8.02 (95%CI=[−18.55, 2.52]) point decrease. The difference in the effect of ETS exposure on verbal IQ for the two cord adduct groups (above and below the median of detectable) was −12.45 points (95%CI=[−25.20, 0.31], p=0.056).

## 4. Discussion

The main finding of the study was that higher prenatal exposure to PAH (measured by cord PAH-DNA adducts), in combination with prenatal ETS exposure, was associated with reductions in verbal and full-scale IQ test scores at age 5, after adjusting for confounding variables. This result is consistent with evidence from our prior studies in NYC that found a significant interaction between cord PAH-DNA adducts and prenatal ETS exposure on cognitive development at age 3 (Perera et al., 2009, 2003, 2005a, 2006, 2007, 2005c, 1998).

The mothers in the study are non-active smokers; however, 70% reported exposure to other people’s tobacco smoke at work or in the home. We did not observe a correlation between ETS and adducts, which is not unexpected given that PAH is one of several thousand different chemicals in tobacco smoke, including neurotoxicants such as carbon monoxide, lead, and arsenic. Based on our prior studies showing significant interactions between PAH-DNA adducts and ETS (Perera et al., 2005a, 2005b, 2007), we assessed the interaction between the two exposures (adducts and ETS). The fact that the interaction term was significant suggests that ETS constitutes other than PAH are combining with PAH from air pollution to cause effects on cognitive development. Because we adjusted for ETS in the models, effectively accounting for the effect of PAH and the many other neurotoxicants in tobacco smoke, we consider PAH-DNA adducts as an indicator of air pollution...
exposure primarily reflecting air pollution exposure from coal burning and motor vehicles.

A strength of the study is the use of a biomarker of exposure to PAH. Because PAH-DNA adduct levels reflect individual variation in exposure, absorption, metabolic activation, and DNA repair, the level of PAH-DNA adducts provides a biologically relevant dosimeter of exposure. However, although we can hypothesize that adduct formation resulting in mutations or apoptosis during critical windows of brain development might be a key mediating event in neurodevelopmental toxicity, here we are considering adducts as a measure of PAH exposure. We note that the cord adduct levels in the Tongliang study were significantly higher than in New York City or Polish newborns, consistent with the higher PAH exposure in Tongliang (Perera et al., 2005c). Specifically, the mean adduct concentration was 45% higher in the Tongliang newborns compared with New York City newborns (Perera et al., 2005c).

A limitation of the study is that we did not have data on postnatal blood levels of PAH-DNA or ETS exposure to allow us to examine the impact of postnatal exposure on 5-year cognitive development. Because the power plant was not shut down until December 2004, the subjects continued to receive seasonal PAH exposure to the plant emissions through May 31, 2003. Since the children were born between March 4 and June 19, 2002, they could have had some exposure to air pollution from the power plant during the first year and a half of life (for 1–3 months in spring 2002 and for 6 months in winter/spring of 2002–2003). However, the plant was not operating for the three and a half years prior to testing at age 5. Moreover, fetal development is considered to be the period of greatest susceptibility to PAH and

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**Fig. 1.** (a–c) Plots of the average fitted values and slopes of the full scale (a), verbal (b) and performance (c) IQ test scores vs. log transformed cord blood DNA adducts at different levels of prenatal environmental tobacco smoke exposure (a, b). (a) The values and slopes were estimated using the interaction models fitted for cord adducts (log transformed), prenatal ETS (hour/day), and their interaction on IQ scores at gestational age of 280 days, Ln(cord lead) of 1.24, mother's age of 25.14 y/o, gender as male and maternal education as equal to or greater than high school. The gestational age of 280 days, Ln(cord lead) of 1.24, mother's age of 25.14 y/o, gender as male and maternal education of ≥ high school were chosen based on the sample median. The models were fitted using all available subjects with ETS data. The range of 0–1 hour/day represents 95% of our study sample. (b) The figures show the estimated change in the relationship between cord adducts and IQ at varying levels of ETS exposure (0, 0.5 and 1 hour/day): the relationship becomes increasingly inverse with greater co-exposure to ETS. The slopes in the figures represent the effect on IQ of a one unit increase of cord adducts in log scale.
other pollutants. Another limitation is the lack of data on cotinine levels (a validated marker of ETS (Seccareccia et al., 2003). However, we have previously reported that, in our New York City cohort, the association between self-reported ETS exposure using a questionnaire similar to the one in the present study and the cotinine assay was highly significant (chi-squared = 48.57, p < 0.001) (Rauh et al., 2004). We also lacked data on other neurotoxicants in ETS (arsenic, carbon monoxide), postnatal data on lead exposure, maternal intelligence, and quality of the home caretaking environment (Bradley et al., 1984). These factors are known or suspected risk factors for neurodevelopmental effects and potential confounders. Nor do we have the data to estimate the relative risk of the other neurotoxicants in ETS compared to that of the PAH from air pollution.

The observed effect on IQ at 5 years of age is likely to be educationally meaningful for some children because compromised intellectual function at an early age has a negative impact on subsequent academic achievement (Drillien et al., 1988).  

5. Conclusion

The present results suggest that, among children living in Tongliang, Chongqing, the combination of in utero exposure to PAH, as measured by PAH-DNA adducts in cord blood, and maternal exposure to ETS adversely affected child IQ. In this city, a coal-fired power plant (since closed down by the government) was the major source of environmental PAHs. Because coal-fired power plants currently produce 75% of China’s electricity and most new plants in China are being built to burn coal, the results from the Tongliang study are relevant to other populations living in China and have implications for worldwide policies concerning energy and public health.

Acknowledgments

We gratefully acknowledge the contribution of Dr. Shuang Wang, Zhiang Li, Qianfei Wang, Lirong Qu, and Berglind Thrastardottir.

References


Table 3

<table>
<thead>
<tr>
<th></th>
<th>Unexposed to cigarette smoke and undetectable cord adduct</th>
<th>Exposed to cigarette smoke and detectable cord adduct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full scale</td>
<td>Counts (%)</td>
<td>Counts (%)</td>
</tr>
<tr>
<td>Above average</td>
<td>2 28.6</td>
<td>9 19.1</td>
</tr>
<tr>
<td>Average</td>
<td>4 57.1</td>
<td>21 44.7</td>
</tr>
<tr>
<td>Below average</td>
<td>1 14.3</td>
<td>17 36.2</td>
</tr>
<tr>
<td>Verbal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above average</td>
<td>2 28.6</td>
<td>7 14.9</td>
</tr>
<tr>
<td>Average</td>
<td>3 42.9</td>
<td>22 46.8</td>
</tr>
<tr>
<td>Below average</td>
<td>2 28.6</td>
<td>18 38.3</td>
</tr>
<tr>
<td>Performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above average</td>
<td>2 28.6</td>
<td>10 21.3</td>
</tr>
<tr>
<td>Average</td>
<td>4 57.1</td>
<td>21 44.7</td>
</tr>
<tr>
<td>Below average</td>
<td>1 14.3</td>
<td>16 34.0</td>
</tr>
</tbody>
</table>

* Below average is defined as IQ < 89. Average is defined as 90 < IQ < 109. Above average is defined as IQ > 110.

With full-scale IQ scores according to exposure to cigarette smoke and detectable cord adducts.


