Air pollution effects on fetal and child development: A cohort comparison in China

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ABSTRACT

In Tongliang, China, a coal-fired power plant was the major pollution source until its shutdown in 2004. We enrolled two cohorts of nonsmoking women and their newborns before and after the shutdown to examine the relationship between prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) and fetal and child growth and development. PAHs were used to measure exposure to air pollution generated by the power plant. Using PAH–DNA adduct levels as biomarkers for the biologically effective dose of PAH exposure, we examined whether PAH–DNA adduct levels were associated with birth outcome, growth rate, and neurodevelopment. Head circumference was greater in children of the second cohort, compared with the first ($p = 0.001$), consistent with significantly reduced levels of cord blood PAH–DNA adducts in cohort II ($p < 0.001$) and reduced levels of ambient PAHs ($p = 0.01$).

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1. Introduction

Air pollution is a serious health concern for the population of China living in urban areas, due to the presence of coal-fired power plants, which currently produce nearly 75% of the country's electricity. Combustion of coal is a major source of air pollution in China ((WADE) World Alliance for Decentralized Energy 2004; Millman et al., 2008). Emissions from the burning of coal contain carcinogenic substances such as particulate matter (PM) and polycyclic aromatic hydrocarbons (PAHs), as well as neurotoxicants such as mercury. While these exposures are harmful for adults, they are particularly detrimental to health during early childhood, as the fetus and child have increased susceptibility to environmental pollutants from increased absorption and slower clearance of toxicants compared to adults (Perera et al., 2006a).

The present study was conducted in the city of Tongliang, which has a population of approximately 810,000 and is situated in a small basin approximately 3 km in diameter (Millman et al., 2008).

A coal-fired power plant located south of the town center operated during the dry season from 1 December to 31 May each year before 2004 to compensate for insufficient hydroelectric power during that time period. This plant was the principal source of local air pollution, in 1995 where nearly all domestic heating and cooking units were converted to natural gas, and motor vehicles were not a major pollution source ((WADE) World Alliance for Decentralized Energy 2004; Chow et al., 2006). Analysis of 72-h average concentrations showed that the highest concentrations of PAHs were found in winter, reflecting the relationship between coal-fired power plant operation and meteorological conditions (Chow et al., 2006).

In May 2004, the Tongliang County Government determined that the shutdown of the power plant would significantly improve local health and have minimal adverse social and economic impacts (Alford and Liebman 2001; (WADE) World Alliance for Decentralized Energy 2004; Chow et al., 2006), and the power plant was closed and replaced by the national grid system of electrical energy. The power plant shutdown provided a unique opportunity to compare air monitoring, biomarker, and health outcome data in successive cohorts of children with or without prenatal exposure to emissions from the coal-fired plant.

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In partnership with Chongqing Children's Hospital, the Columbia Center for Children's Environmental Health has carried out two prospective cohort studies in Tongliang, China to examine the impact of exposure to emissions from the coal-fired power plant on children's health. The first cohort was recruited prior to the power plant shutdown in 2002, and the second cohort was recruited following the shutdown in 2005. Here we test the hypothesis that the shutdown of the power plant has had a significant beneficial health impact on children born in the Tongliang area. We anticipated that the levels of outdoor emissions, and in particular, PAH, would decrease following the power plant shutdown, and translate to improved health outcomes.

PAH–DNA adducts are widely used as a risk marker because they provide an informative individual biologic dosimeter and risk marker for exposure to PAH. Therefore, we expected to find lower cord PAH–DNA adduct levels and more favorable birth/child neurodevelopment and physical outcomes in the second cohort compared to children in the first cohort enrolled when the power plant was still operational. PAH–DNA adducts also take into individual susceptibility, reflecting individual variation in exposure, absorption, metabolic activation, and DNA repair (Tang et al., 2001; Perera et al., 2007). The lipid soluble characteristic of PAHs allows these molecules to be stored in the mother's fat tissue and further transferred to the developing fetus, so PAH metabolism may vary based on additional factors such as the mother's nutritional status and polymorphic characteristics of PAH metabolism pathways. These factors are being evaluated for influence on fetal/child physical and neurodevelopment in a subsequent cohort recruited in 2007 in Tongliang to investigate the long term benefits of shutting down the Tongliang power plant.

2. Methods

2.1. Air monitoring

Integrated 72-h PAH samples were collected with two Mini-Vol samplers (Airmetrics, Eugene, OR, USA) at three sites in Tongliang between March 2002 and February 2003 and between March 2005 and February 2006. Details of sampling parameters and locations are recorded in our previous publication (Chow et al., 2006). Data on B[a]P from the months of December to May, the active period of the power plant in 2002, were used to calculate the averages from 3 monitoring stations. However in 2002, B[a]P data are lacking due to malfunctioning samplers caused by the local damp weather. B[a]P data is available for each month at sites A, B, and C in 2005, but during 2002 are unavailable across all 3 sites at different periods. Therefore the yearly average of B[a]P levels are calculated from periods where data from both years were available. Concentrations of PAHs (ng/m^3) were analyzed by thermally desorbing a quartz fiber filter strip in the injection port of a gas chromatography (GC) system followed by GC separation and mass spectrometric detection. The method details and performance characterization are described elsewhere (Ho and Yu, 2004; Ho et al., 2008).

2.2. Study subjects

In the 2002 cohort, the subjects were 150 children born to nonsmoking Chinese women who gave birth between 4 March 2002 and 19 June 2002 at four hospitals in Tongliang: the Tongliang County Hospital, the Traditional Chinese Medicine Hospital, the Tongliang Maternal Children's Health Hospital, and the Bachuan Hospital. In the 2005 cohort, the subjects were 158 children born at the same hospitals from 2 March 2005 to 23 May 2005. The women were selected using a screening questionnaire when they checked in for delivery. Eligibility criteria included current nonsmoking status, 20 years of age or older, and residence within 2.5 km of the Tongliang power plant. Only one woman declined to participate. All other eligible women agreed to enter the study and gave informed written consent by completing a form approved by the Columbia University Institutional Review Board and Chongqing Medical University, which are available upon request. The demographic characteristics of the two cohorts are presented in Table 1.

2.3. Personal interview

A 45-min questionnaire was administered by a trained interviewer after delivery. The questionnaire elicited demographic information, lifetime residential history (location of birth and duration of residence), history of active and passive smoking (including number of household members who smoke), occupational exposure, medication use, alcohol consumption during each trimester of pregnancy,

Table 1
Demographics.

	Cohort I (2002) (n = 150)[a]	Cohort II (2005) (n = 158)[a]	p-value[b]
Maternal age (years)	25.3 ± 3.2	27.8 ± 4.6	<0.001
Maternal ETS (h/day)	0.4 ± 1.1	0.3 ± 0.5	0.23
Maternal height (cm)	157.9 ± 3.8	158.2 ± 3.9	0.54
Maternal pre-pregnancy weight (kg)	49.6 ± 5.8	51.8 ± 6.1	0.002
Maternal head circumference (cm)	54.5 ± 1.3	55.3 ± 1.3	<0.001
Caesarian delivery (%)	53.7	67.5	<0.001
Gestational age (days)	277.8 ± 10.9	277.0 ± 8.8	0.48
Newborn birth weight (g)	3337.5 ± 388.1	3406.0 ± 399.8	0.13
Newborn birth length (cm)	50.3 ± 1.7	50.3 ± 1.5	0.83
Newborn head circumference (cm)	33.8 ± 1.1	34.2 ± 1.3	0.001
Sex of newborn (% female)	49.6	45.2	0.35

[a] Values are mean ± SD or percent.
[b] Simple *t*-test. *p*-values for mean comparisons are obtained using the *t*-test. *p*-values for percentage comparisons are obtained using the chi-squared test.

and consumption of PAH-containing meat (frequency of eating fried, broiled, or barbecued meat during the last 2 weeks). Socioeconomic information related to income and education was also collected.

2.4. Biological sample collection and analysis

Maternal blood (10 mL) was collected within 1 day postpartum, and umbilical cord blood (40–60 mL) was collected at delivery. Samples were transported to the field laboratory at the Tongliang County Hospital immediately after collection. Blood samples, the buffy coat (granulocytes and leucocytes), packed red blood cells, and plasma were separated and stored at −70 °C. Details of laboratory methods have been described previously (Tang et al., 2008).

2.5. DNA adducts

B[a]P is a PAH measured to estimate the overall PAH concentration in a sample. B[a]P–DNA adducts were analyzed in extracted white blood cell (WBC) DNA with a modified method using high performance liquid chromatography (HPLC)/fluorescence detection. This assay is a sensitive and specific method for measuring B[a]P–DNA adducts in WBCs from individuals exposed to B[a]P (Bartsch, 1996) and has a 12% coefficient of variation (CV) (Tang et al., 2006). As such, the specific PAH–DNA adducts measured in this study are B[a]P-DNA adducts. The detection limit used for B[a]P DNA adducts was 0.25 adducts per 10^8 nucleotides.

2.6. Measurement of birth outcomes and physical development

Birth weight, birth length, and head circumference were measured immediately after parturition. Head circumference of infants delivered with Cesarean was measured more than once following birth and the average of the measurements were taken. Information abstracted by the research workers from mothers' and infants' medical records after delivery included date of delivery; gestational age at birth (based on the last menstrual period); infant sex, birth weight, length, head circumference, maternal height, pre-pregnancy weight, and total weight gain; complications of pregnancy and delivery; and medications used during pregnancy.

2.7. Measurement of child neurodevelopment

The experimental approach and methods used in this investigation and the comparison of the two cohorts have been presented elsewhere (Perera et al., 2008a), so only a brief summary is given here. Two-year-old children in the cohort were administered the version of the Gesell Developmental Scale (GDS) for 0- to 3-year-old children adapted to the Chinese population (Beijing Mental Development Cooperative Group, 1985). This standardized test is used in China for measuring IQ as it is the only test of its kind approved and endorsed for use by the Chinese Pediatric Association. The drop-out rate at 24 months follow up was 11.3% in the 2002 cohort and 22.8% in the 2005 cohort. Each child is assigned a DQ (development quotient) in each of four areas: motor, adaptive, language, and social. The standardized mean (±SD) of the DQ is 100 ± 15; a score < 85 indicates developmental delay (Hudon et al., 1998). Testing was conducted by physicians in the same group who were certified in the GDS to maximize reliable assessment and valid interpretation. Therefore, both inter-examiner and intra-examiner variability were minimal.

3. Results

The demographic, exposure, and birth outcome characteristics for the mother–newborn pairs from cohorts I and II are compared in Table 1. Maternal ETS exposure, maternal height, and gestational age did not differ between the two cohorts. Maternal age ($p < 0.001$), maternal weight before pregnancy ($p = 0.002$), maternal head circumference ($p < 0.001$), and Caesarian delivery status ($p < 0.001$) were significantly different between the two cohorts and therefore adjusted for in the statistical models. Growth rate for height was higher in cohort 1 compared to cohort 2, but this difference was not statistically significant. Growth rate in weight was also higher in cohort I.

3.1. Air monitoring

Air pollution was measured in order to examine the reduction of emissions after the power plant shutdown (Chow et al., 2006) and to determine a positive association to PAH–DNA adducts in cord blood (Gallagher et al., 1993; Perera et al., 2005; Tang et al., 2006; Perera et al., 2008b; Kelvin et al., 2009; Herbstman et al. 2012). The total B[a]P concentrations determined in 2002 and 2005 are shown in Fig. 4 (panel 1), and classified into the months December–May and June–November, with the period December–May coinciding with the period when the power plant was open in 2002 and the seasonal variability of PAH is high. Decreases were found in B[a]P from 13.14 ng/m^3± in 2002 to 9.14 ng/m^3 in 2005. B[a]P derives mainly from fossil fuel combustion, which explains the significant reduction in B[a]P during the active months of December to May in 2002 and 2005. These data indicate improvement of air quality in Tongliang, especially with respect to PAH exposure, after the closure of the coal power plant in 2004. This is consistent with our findings in PAH–DNA adduct levels.

3.2. DNA adducts

PAH–DNA adducts reflect individual variation in exposure, absorption, metabolic activation, and DNA repair; therefore adduct levels in umbilical cord white blood cells are used as an integrated biological dosimeter that has been associated with developmental impairment (Harris, 1985; Belinski et al., 1987; Weston et al., 1988; Perera et al., 2004; Perera et al., 2005; Tang et al., 2006; Perera et al., 2008b). PAH–DNA adduct levels of the two cohorts are shown in Table 2. Since the PAH–DNA adducts were not normally distributed, the more conservative Mann–Whitney test was used to compare the PAH–DNA adduct levels in the two cohorts. There is a significant reduction of PAH–DNA adducts in the 2005 cohort (0.33 ± 0.140 adducts/10^{-8} in 2002, vs. 0.20 ± 0.08 in 2005 $p = <0.001$) reflecting the significant effect of emission reduction ($p = < 0.01$). Furthermore, a linear regression analysis was applied to adjust for other sources of exposure including ETS and dietary PAH. This analysis also indicated a significant reduction; however, the contribution of ETS and dietary PAH to the model was not significant and therefore was not included. After adjusting for cigarette smoke and food PAH, average cord adduct level in cohort II

was 0.128 adducts per 10^8 nucleotides (95% CI=(0.098, 0.159)) lower than that in cohort I.

3.3. Birth outcomes

PAH–DNA adduct levels are hypothesized to be inversely related to birth outcome. Comparison of mean birth weight, birth length, and head circumference at birth showed that head circumference was significantly larger for children in cohort II where PAH–DNA adducts had been reduced (Table 1). In cohort I, high adduct levels were associated with reduced birth head circumference after adjusting for ETS, gender, mother's weight before pregnancy, height of mother, gestational age, mother's head circumference, and Caesarian status ($p = 0.057$). This association was no longer seen in the 2005 cohort (Table 3).

3.4. Growth rate

For each cohort, infants were monitored post- delivery for developmental trends that may have resulted from pre- and post-natal exposure to air pollution. Growth rate was compared for weight, height, and head circumference for up to 30 months of age from cohort I in 2002 before the power plant shutdown and cohort II in 2005 after the power plant shutdown. Interestingly, Table 4 shows significant inverse associations between DNA adducts and weight in cohort I at age 18, 24, and 30 months but no association in cohort II.

Contrary to our hypothesis, using a random effects model and after adjusting for relevant covariates (Table 4 footnotes), the growth rate for weight at 18 and 24 months in cohort I (1.4322 kg/6 mo.) was greater compared to cohort II (0.8063 kg/6 mos) as seen in Fig. 1. These results can be attributed to a phenomenon known as catch-up growth as a result of a transient period of growth inhibition in cohort I (Hirvonen, 2013). Similarly, the growth rate for height was also found to be greater at 30 months for cohort I (4.8367 cm/6 mos) compared to cohort II (4.0432 cm/6 mos) as seen in Fig. 2. However, these trends need to be verified within a larger cohort. There was only a significant difference between the two cohorts in initial birth head circumference but not a significant difference in overall growth rate between cohort I and cohort II (Fig. 3). The head circumference trajectories for the 2002 and 2005 cohorts are parallel but the means are consistently lower for the 2002 cohort.

3.5. Neurodevelopment

Air pollution was hypothesized to have negative effects on neurological development. Findings from the present cohort regarding this hypothesis have been reported previously and published elsewhere (Perera et al., 2008a; Perera et al., 2009). Briefly, the benefits of reduced exposure on neurodevelopment were determined by comparing the two cohorts with respect to the GDS scores at age two. As previously described, the frequencies of developmental delay in all DQ areas except for language were reduced in 2005 compared with 2002 (Perera et al., 2008a; Perera

Table 2
The PAH–DNA adducts level in the 2002 and 2005 cohorts (adducts/10^8 nucleotides).

	2002			2005			Test
	Mean ± SD	Median	N	Mean ± SD	Median	N	
PAH–DNA adduct level							Mann–Whitney
All subject	0.330 ± 0.140	0.321	131	0.200 ± 0.080	0.125	140	<0.001
% detectable							Chi-squared
All subject	79.400	1.000	131	47.100	0	140	<0.001

Table 3
Association between cord blood PAH–DNA adducts (dichotomized high/low)[a] and birth outcomes[b] in cohorts I and II.

		Birth weight		Birth length		Birth head circumference	
		β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Cohort I (2002)	Cord Adduct Level (High/low)	−0.007 (−0.049, 0.035)	0.74	−0.001 (−0.013, 0.011)	0.89	−0.011 (−0.023, 0.00034)	0.057
Cohort II (2005)	Cord Adduct Level (High/low)	−0.015 (−0.060, 0.030)	0.51	0.008 (−0.004, 0.020)	0.18	−0.006 (−0.020, 0.007)	0.36

[a] Adducts dichotomized as high/low based on the median of detectable values (0.36 adducts/10^8 nucleotides for cohort I and 0.27 adducts/10^8 nucleotides for cohort II).
[b] Birth outcomes are log transformed. Models involving birth weight and birth length adjusted for ETS, gender, mother's weight before pregnancy, height of mother, and gestational age. Models involving birth head circumference additionally adjusted for mother's head circumference and Caesarian status.

et al., 2009). For motor area, there was a significant difference in the frequency of delay ($p = 0.017$). Multiple regression analysis showed that in the 2002 cohort, cord adducts were significantly inversely associated with the DQ in the motor area after adjusting for covariates (adjusted $\beta = -16.01$; 95% CI, −31.30 to −0.72; $p = 0.043$) (Perera et al., 2008a). Cord adducts were also associated with the average DQ in 2002, (adjusted $\beta = -14.58$; 95% CI, −28.77 to −0.37, $p = 0.047$). In contrast, the 2005 cord adducts were not significantly associated with any of the DQs after adjusting for the same covariates, (for motor area DQ, $\beta = -5.90$; 95% CI, −24.96 to 13.17; $p = 0.546$) and average DQ ($\beta = -12.38$; 95% CI, −28.95 to 4.21; $p = 0.146$) (Perera et al., 2008a). Similarly, when the Gesell DQ was dichotomized into high/low scores and results of 2002 and 2005 were compared using Fisher's exact test, the percentage of subjects categorized as delayed for the motor area was significantly lower in 2005 (4.1%) than in 2002 (88%) (Perera et al., 2008a) (Fig. 4).

These findings confirm the correlation between PAH–DNA adducts due to air pollution and its effect on the developing fetus *in utero* and during the critical period of early childhood.

4. Discussion

4.1. Air pollution

The coal-fired power plant located in downtown Tongliang was estimated to have burned 24,000 tons of coal per year and thus was the county's principle source of air pollution. During the operation season, the plant produced vast quantities of ambient air pollution which included PM, PAHs, carbon dioxide (CO_2), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and heavy metals. Around 2000 mg/m^3 (40 tons/day) of particles were emitted compared to the U.S standard of 250 mg/m^3 (Millman et al., 2008). The plant's closure was the major factor in benefitting fetal growth and later childhood development, as indicated by air monitoring data which showed reductions in atmospheric concentrations of B [a]P over the study period (Chow et al., 2006). PAH $_5$ data collection was initiated at the beginning of March 2002, when the pre-childbirth women were recruited into the study, and completed the subsequent year. Measurements taken during the peak period when the power plant was active in 2002 were assumed to be comparable to the previous year during actual fetal development (Chow et al., 2006). Due to the nature of the air monitoring devices, excessive levels of air pollution resulted in a failure to measure PAH levels for 28% of the total months. There was a large in decrease in concentration of B[a]P between the active months of the power plant compared to inactive months. In addition to high levels of B[a]P attributed to the operation of the power plant, meteorological conditions during the winter months contributed to an even greater increase of pollutant levels. Cold and dry weather during the winter season lead to lower precipitation and stagnant air that enhance pollutant accumulation (Chow et al., 2006). This phenomenon explains the higher pollution levels during the winter months in 2005 from alternate sources such as diesel vehicle emissions, residential wood burning, and more fuel combustion activities from the region despite the shutdown of the power plant (Chow et al., 2006).

Table 4
Results of multiple regression analyses of growth outcome and PAH–DNA adducts at birth, 18, 24, and 30 months (M) after birth.

	2002[d]		2005[d]		All[e]		All[f]	
	β (n)	p-value	β (n)	p-value	β (n)	p-value	β (n)	p-value
HC[a]								
Birth	−0.011 (112)	0.057*	−0.022 (135)	0.271	−0.026 (247)	0.117	−0.006 (247)	0.165
18M	−0.012 (109)	0.085	0.006 (107)	0.684	−0.022 (217)	0.142	−0.005 (217)	0.178
24M	−0.006 (118)	0.188	0.015 (104)	0.358	−0.019 (221)	0.167	−0.004 (221)	0.242
30M	−0.005 (118)	0.311	0.011 (97)	0.551	−0.022 (215)	0.145	−0.004 (215)	0.262
WT[b]								
Birth	−0.007 (112)	0.738	−0.085 (139)	0.205	−0.040 (251)	0.470	−0.008 (251)	0.577
18M	−0.048 (110)	0.030*	−0.003 (110)	0.956	−0.236 (221)	0.000*	−0.052 (221)	0.001*
24M	−0.041 (118)	0.027*	0.089 (107)	0.118	−0.167 (223)	0.001*	−0.034 (223)	0.011*
30M	−0.040 (119)	0.049*	0.059 (100)	0.351	−0.046 (219)	0.426	−0.006 (219)	0.693
HT[c]								
Birth	−0.001 (112)	0.890	−0.008 (136)	0.634	0.012 (248)	0.426	0.003 (248)	0.492
18M	−0.005 (110)	0.483	0.008 (110)	0.658	0.007 (221)	0.661	0.003 (221)	0.535
24M	−0.007 (118)	0.281	0.016 (107)	0.371	−0.010 (223)	0.570	0.000 (223)	0.950
30M	−0.006 (119)	0.437	0.026 (100)	0.143	0.033 (219)	0.100	0.010 (219)	0.047*

Gestational age was additionally considered as a covariate for birth outcome analysis.
[a] Adjusted for ETS, gender, mother's weight before pregnancy, mother's height, mother's head circumference, and Caesarian status.
[b] Adjusted for ETS, gender, mother's weight before pregnancy and mother's height.
[c] Adjusted for ETS, gender, mother's height and mother's weight before pregnancy.
[d] Adducts were dichotomized as high/low at the median of the detectable of the 2002 cohort, which is 0.356 adducts/10^8 nucleotides (high:>0.355, low:<=0.355).
[e] Analyses were done using all subjects from the 2002 and 2005 cohort, with cord adducts modeled in the original scale and covariates specified as above. The discrepancy between the subject's numbers in the ALL models and the sum of the subject's numbers in the 2002 and 2005 models is due to growth outcome data correction in Spring 2008.
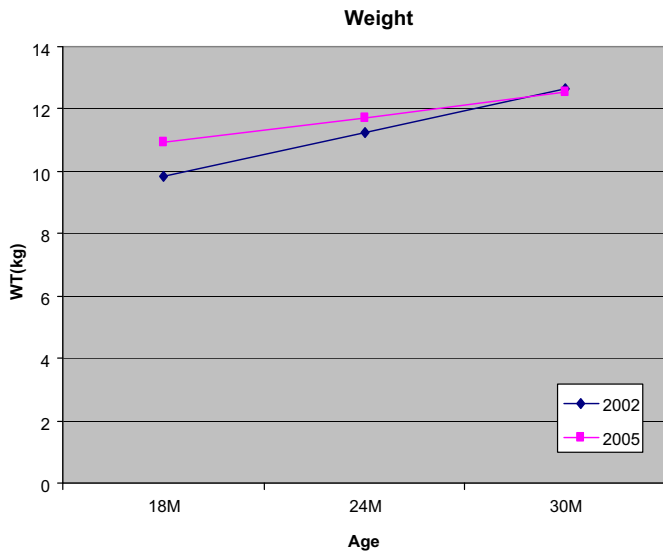[f] Analyses were done using all subjects from the 2002 and 2005 cohort, with cord adducts modeled as log transformed and covariates specified as above. The discrepancy between the subject's numbers in the ALL models and the sum of the subject's numbers in the 2002 and 2005 models is due to growth outcome data correction in Spring 2008.

Weight

Fig. 1. Growth Rate for Weight from 18 to 30 months in cohorts I and II.
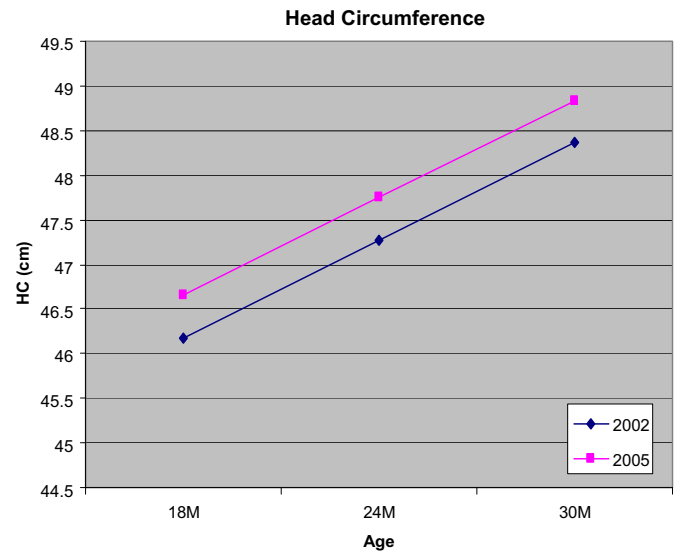
Head Circumference

Fig. 3. Growth rate for head circumference from 18 to 24 months in cohorts I and II.

4.2. Birth outcomes

The detectable PAH–DNA adducts in the umbilical cord decreased in 2005 (47.1%) compared to 2002 (79.4%), which was consistent with our findings of decreased ambient concentrations of B[a]P. This association indicates the strength of B[a]P − DNA adducts as a biological dosimeter of PAH exposure, as PAH is a common carcinogen found in air pollution. Prior studies, including our own, have shown that fetal growth has been associated with a number of environmental exposures including transplacental exposure to ETS and PAH (Perera et al., 1999; Tang et al., 2006). Head circumference, birth weight, and birth length are the most commonly measured parameters of fetal growth and development. In the present study, reduced head circumference, as a result of increased B[a]P adducts seen in cohort I, was no longer observed in infants who were prenatally unexposed in cohort II, after adjusting for potential confounders (Tang et al., 2008). It is important to note that the initial birth weight and height for infants in the 2002 cohort were lower than for those in the 2005 cohort, though the differences were not significant. These findings are also of potential

concern because several previous studies have reported a correlation between overall reduced fetal growth and adverse cognitive outcomes (Chaikind and Corman, 1991; Matte et al., 2001). The increased sensitization of head circumference, versus birth weight and height, can be explained by the developing central nervous system being extremely vulnerable to toxic chemicals. The fetal brain undergoes tremendous growth and differentiation that is sensitive to circulating neurotoxins, as the blood brain- barrier is not fully developed (Perera et al., 1999). Understanding the neurodevelopment effects due to PAH exposure in combination with our findings of reduced head circumference suggests that a compromised head circumference may be indicative of poorer neurodevelopment outcomes (Desch et al., 1990). Prior studies have concluded that even within the range of children born at term, pre- and post-natal growth in body size are associated with individual differences in cognitive abilities. A larger head circumference at birth is associated with better childhood learning capabilities later in life (Heinonen et al., 2008; Veena et al., 2010).

4.3. Early childhood growth rate

The reduced head circumference measured at birth for infants in the 2002 cohort continued to be of concern up to the last measurement taken at 30 months. There was no significant difference in head circumference growth rate between the two cohorts, resulting in the persistence of the smaller head circumference of the 2002 cohort into childhood. Interestingly, the difference in growth rate for weight seen at 18 and 24 months was significantly greater for the 2002 cohort. This allowed infants from 2002 to "catch-up" to those from 2005, such that were no significant differences in weight between the two cohorts at 30 months. Similarly, the growth rate for height was significantly greater for the 2002 cohort, which resulted in a greater height for the 2002 cohort compared to the 2005 cohort at 30 months. These inconsistent results may be due to unmeasured paternal contributions. Studies have shown that the father plays an equally critical role to mothers in determining fetal and child growth, further emphasizing the importance of the genetic component in infant growth rate (Magnus et al., 2001; Jaquet et al., 2005). Additionally, post natal nutritional intake is known to play a key role in physical development (Guilloteau et al., 2009; Collins et al., 2010). Further studies using a larger study population, measurement of nutritional intake,
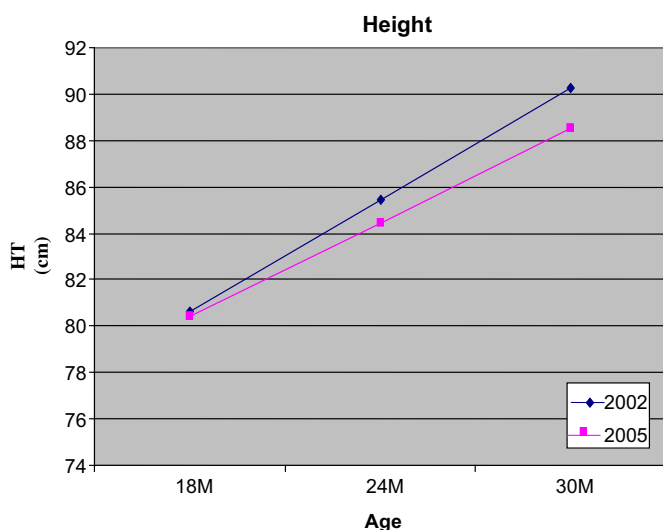
Height

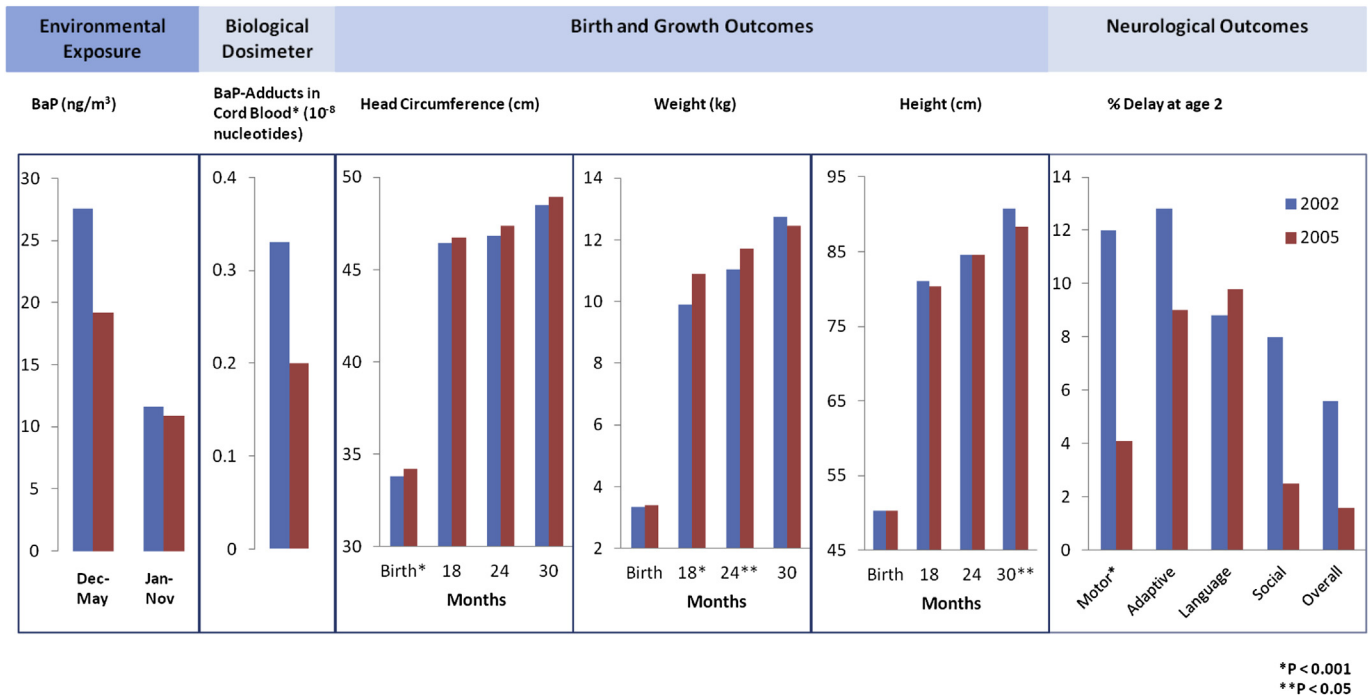Fig. 2. Growth rate for height from 18 to 30 months in cohorts I and II.

Fig. 4. **Summary of comparisons for environmental exposure, biological dosimeter, birth, growth, and neurological outcomes**. Panel 1: Average ambient B[a]P for operational and non-operational seasons in 2002 and 2005. Panel 2: Mean PAH–DNA adducts from all subjects in 2002 and 2005. Panel 3: Multiple regression analyses of growth outcome and PAH–DNA adducts for head circumference in 2002 and 2005. Panel 4: Multiple regression analyses of growth outcome and PAH–DNA adducts for weight in 2002 and 2005. Panel 5: Multiple regression analyses of growth outcome and PAH–DNA adducts for height in 2002 and 2005. Panel 6: Gesell DQ scores dichotomized into high/low and results were compared using Fisher's exact test for 2002 and 2005.

and paternal measurements are warranted to explore reasons that may help explain these results.

4.4. Neurodevelopment

The finding of increased developmental delays in the 2002 cohort was consistent with prior experimental data showing prenatal B[a]P exposure resulted in adverse neurodevelopment effects in offspring (Archibong et al., 2002; Wormley et al., 2004a,b; Perera et al., 2008a). B[a]P has been found to decrease motor activity and responsiveness to sensory stimuli as well as increase neuromuscular, physiological and autonomic abnormalities (Saunders et al., 2002; Wormley et al., 2004a,b). Significant correlations between PAH–DNA adduct levels and DQ decrements were found in the motor area and average DQs among 2 year old children exposed *in utero* during the power plant operational season. More importantly, these correlations were not seen for children monitored in the 2005 cohort after the power plant shutdown (Perera et al., 2008a). Developmental delays typically indicate that a child is not meeting certain milestones for his/her age which may have a later impact on school performance (Drillien et al., 1988). According to the Gesell Developmental Scale used to test the children, this type of muscle coordination suggests a delay in the child's ability to turn pages in a book, stack up to 6–7 cubes, climb steps with or without assistance, or perform other similar activities (Beijing Mental Development Cooperative Group, 1985). Associations between all other DQ domains including adaptive, language, and social areas such as recognizing one's name or forming at least three word sentences showed an inverse relationship with PAH–DNA adduct levels in the 2005 cohort, albeit not significantly (Beijing Mental Development Cooperative Group, 1985). This suggests that greater benefits may be observed in the 2007 cohort as stored concentrations of PAH compounds that are transferable to the fetus will continue to decline. Our cohort studies in New York City and Krakow

have provided evidence that prenatal exposure to PAH is associated with reduced IQ at age 5 (Kelvin et al., 2009; Perera et al., 2009).

5. Conclusion

The prospective cohort conducted in 2002 led to the shutdown of the coal-fired power plant in Tongliang in 2004. This provided a unique opportunity to further evaluate the benefits of reduced exposure to air pollution by conducting a second prospective cohort study in 2005. This cohort comparison study has the advantage of being the first to evaluate the impact of a coal-fired power plant shutdown on children. Furthermore, the use of B[a]P-DNA adducts as our biomarker of exposure allowed us to quantitatively measure the biologically effective dose of B[a]P for newborns in cohort I and cohort II. Infants were monitored after birth for up to 30 months, providing data on the effects of pre- and post natal exposure on growth rate. However, the study was limited by the modest number of study subjects (150 in cohort I and 158 in cohort II) and therefore the ability to control for other environmental interactions. Nonetheless, averaged air pollution data showed a significant positive correlation with increased B[a]P DNA adduct levels. Prior studies have linked PAHs and PAH–DNA adducts with developmental deficits and increased risk of cancer in children in China and other countries (Perera et al., 2005; Choi et al., 2006; Mielzynska et al., 2006; Perera et al., 2006a; Perera et al., 2006b; Tang et al., 2006; Masters et al., 2007; Perera et al., 2007; Ruchirawat et al., 2007; Tuntawiroon et al., 2007; Perera et al., 2008a; Bocskay et al., 2005; Bocskay et al., 2007; Perera et al., 2007; Kelvin et al., 2009; Herbstman et al., 2012). Further studies are needed to examine the potential health effects of modern "clean power plants". However, these instillations should also be evaluated for possible environmental effects. In addition to the unique opportunity to examine subjects before and after the closure of the power plant, our continued work with a 2007 cohort in Tongliang will further

emphasizes the benefits of reduced exposure. The findings of this study are encouraging in that direct governmental interventions to remove a polluting coal-burning source can have rapid and direct benefits to children's health (Barker, 2004). This in turn is a strong motivation for China to further invest in renewable and energy-efficient fuels, a necessity for its future.

Acknowledgments

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