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Prenatal Cocaine Exposure: Drug and Environmental Effects at 9 years

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Abstract

Objective—To assess school age cognitive and achievement outcomes after prenatal cocaine exposure, controlling for confounding drug and environmental factors.

Study design—At 9 years, 371 children (192 cocaine exposure, CE; 179 non-exposure, NCE) were assessed for IQ and school achievement in a longitudinal, prospective study from birth. An extensive number of confounding variables were controlled, including quality of caregiving environment, polydrug exposure, lead, iron deficiency anemia (IDA), and foster/adoptive care.

Results—CE predicted poorer Perceptual Reasoning IQ with a linear relationship of the concentration of the cocaine metabolite, benzoylecgonine, to degree of impairment. Effects were mediated through birth head circumference, indicating a relationship with fetal brain growth. Negative effects of alcohol, lead, and marijuana exposure and positive effects of home environment were additive. Children with CE in foster/adoptive care had better home environments and lower lead levels. School achievement was not affected.

Conclusions—There were persistent teratologic effects of CE on specific cognitive functions and additive effects of alcohol, lead, marijuana, IDA, and home environment. Documenting environmental factors in behavioral teratology studies is important because in this sample, CE was associated with better home environments and lower environmental risk for a substantial number of children.

Keywords

Lead; alcohol; marijuana; iron deficiency anemia; home environment; cognition; school achievement; poverty; behavioral teratogen

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Approval/Compliance: Compliance was met in accordance to Health Insurance Portability & Accountability Act of 1996 (HIPPA). Written consent was obtained from the parent/guardian of children who served as subjects of our investigation and, when appropriate, from the subjects themselves. Subjects were protected by a writ of confidentiality (#DA-04-03).[13]

Hundreds of thousands of children prenatally exposed to cocaine in the 1980s and 1990s have now reached school age, but there is little information on their cognitive outcomes.(1) Animal studies document significant negative effects of fetal exposure, including alterations in brain structure and function and deficits in cognitive processes, especially attention, spatial working memory and the ability to acquire new learning.(2,3) Human studies are more difficult to conduct because of variability in timing, dose, and duration of exposure and numerous confounding factors. These include low socioeconomic status; maternal psychological distress, lower IQ and education; polydrug exposure; poor prenatal care; iron deficiency anemia and lead exposure.(4) Out of home placement is common, and there is often significant, selective attrition in longitudinal studies.

Recent large, well-controlled studies with high retention rates demonstrate negative effects of prenatal cocaine exposure on fetal growth, birthweight, and infant behavior.(5,6) Specific language and cognitive deficits have been reliably found in preschool assessments.(7–10) However, there are few methodologically adequate reports at school age, when earlier problems may resolve, or become more pronounced in response to greater cognitive demands, and their findings are inconsistent.(11,12) The present study investigated cognitive outcomes and school achievement in a large sample of children followed from birth after prenatal CE, with control for confounding factors.

METHODS

Subjects

Subjects included 9-year-old children enrolled in a longitudinal study from birth (September 1994–June 1996). Mothers were recruited at a large urban county teaching hospital from a high-risk population screened for drug use. Women at high risk for drug use due to lack of prenatal care, behavior suggesting intoxication, a history of prior involvement with the Department of Human Services, or self-admitted use, were given toxicology screenings. Maternal and infant urine samples were obtained immediately before or after labor and delivery and analyzed for cocaine metabolites, cannabinoids, opiates, phencyclidine, and amphetamines, using the Syva Emit method (Syva Co, Palo Alto, California), followed with gas chromatography. Meconium collected from infants' diapers was analyzed for drug metabolites, including benzoylecgonine, meta-hydroxybenzoylecgonine, cocaethylene, cannabinoids, opiates, phencyclidine, amphetamines, and benzodiazepines. Screening assays were conducted using polarization immunoassay reagents (Fluorescence Polarization Immunoassay, U.S. Drug Testing Laboratories, Inc, Des Plaines, Illinois). Cutoff levels were: cocaine and metabolites, 25 ng/g; opiates, 25 ng/g; amphetamines, 100 ng/g; phencyclidine, 25 ng/g; and tetrahydrocannabinol, 25 ng/g. Confirmatory assays were conducted. Specificity for both urine and meconium cutoffs was 99%.

CE was identified if the mother reported use during pregnancy or if her urine or her infant's urine or meconium were positive. Infants were considered negative if self-report, urine, and meconium assays were all negative. Of 647 mothers and infants identified, 54 were excluded (20 CE, 34 NCE), for no meconium (15), Down syndrome (2), maternal psychiatric history (16), primary heroin use (2), HIV positive (5), maternal IQ < 70 (1), fetal alcohol syndrome (1), maternal age < 19 (2), infant medical illness (3), maternal chronic illness (4), and other (3). 155 women refused to participate (49 CE and 106 NCE); 23 (9 CE, 14 NCE) did not come to the enrollment visit. 415 women and infants were enrolled (218 CE, 197 NCE).

Procedures

After birth, a research assistant interviewed mothers about prenatal drug use.(13) To quantify use, they were asked to recall frequency and amount for the month prior to and for each trimester

of pregnancy. The number of tobacco cigarettes and marijuana “joints” smoked, and the number of drinks of beer, wine, or hard liquor per day were computed, with each drink equivalent to 0.5 oz of absolute alcohol. For cocaine, the number of “rocks” consumed and the amount of money spent per day were noted. For each drug, frequency of use was recorded on a Likert-type scale ranging from 0 (not at all) to 7 (daily use), converted to reflect the average number of days per week a drug was used, except for cigarettes, collected as the number smoked per day. Frequency was multiplied by the amount used per day to compute an average use score for the month prior to pregnancy and for each trimester. This score was then averaged to obtain a total score. Measures were updated at each follow-up.

Maternal education level and socioeconomic status (on public assistance vs. none) were determined. The Peabody Picture Vocabulary Scale-Revised (PPVT-R),(14) and the block design and picture completion subscales of the WAIS-R,(15) were used to obtain measures of maternal vocabulary, and nonverbal intelligence. The General Severity Index (GSI), a summary scale of the Brief Symptom Inventory,(16) measured psychological distress. Maternal race, age, parity, number of prenatal visits, infant gestational age, birth weight, length, head circumference, and Apgar scores were taken from hospital records. The Hobel neonatal risk score(17) measured neonatal risk condition.

At two and four years, children participated in a separate study of lead exposure and IDA.(4) Blood samples could not be obtained from some children due to parental refusal, inability to draw blood without undue stress, child sickness or logistical difficulties. The numbers of subjects with valid blood measures at two and four years were 143 and 274, respectively. For the 122 children seen at both times, measures were averaged. A greater percentage of African-American and married women, and a lower percentage of foster parents, consented for blood collection. Elevated blood lead values were defined as ≥ 10 mg/dL at either 2 or 4 years.

Hematologic assessments included hemoglobin (Hb), mean corpuscular volume (MCV), % transferrin saturation (TS), serum ferritin (SF) and lead. Abnormal blood values for iron deficiency with and without anemia followed the recommendations of the American Academy of Pediatrics and prior studies(18,19) the cutoff values at two years (Hb < 11.0 g/dl, MCV. 70 # m³, TS. 10 %, SF. 12 # g/liter); and at four (Hb < 11.2 g/dl, MCV. 73 # m³, TS. 12%, SF. 12 # g/liter).

At 9 years, examiners unaware of child cocaine status individually administered the Wechsler Intelligence Scale for Children - Fourth Edition (WISC IV),(19) and the Woodcock Johnson – III Tests of Achievement (WJTOA-III),(20) to measure math, reading, and written language. The WISC-IV yields a full Scale and 4 summary IQs (Verbal Comprehension, Perceptual Reasoning, Processing Speed, Working Memory). The elementary school version of the Home Observation of the Environment (HOME)(21) was given to the caregiver in an interview to assess quality of caregiving. Child placement (with birth mother/relative or foster/adoptive caregiver) was noted, and current caregiver data were updated.

Statistical Analyses

We conducted statistical analyses in several steps. Multivariate analyses of variance (MANOVA) were conducted on unadjusted values to assess group differences followed by linear regressions to assess specific drug effects. Covariates related to outcomes at $p < .20$ were evaluated hierarchically, accounting for demographic, environmental, and medical factors first, and retaining all variables at $p < .10$. Order of entry was: HOME, maternal age, parity, number of prenatal care visits, maternal years of education, marital status, socioeconomic status, birth mother and current caregiver PPVT-R, WAIS-R block design and picture completion scores, foster/ adoptive care status, birth mother and current caregiver psychological distress, prenatal

and concurrent cigarette, alcohol, marijuana, and CE. Sex and race did not differ by cocaine status, and were tested as moderators through interaction terms.

To assess the relationship of lead exposure and IDA to outcomes relative to cocaine/polydrug exposure and environmental factors, hierarchical multiple/logistic regressions were performed, using the same evaluation of covariates, for 271 children with blood samples. Analyses were repeated using the concentrations of cocaine metabolites in meconium as the exposure variable. Infant growth measurements at birth and neonatal medical conditions(5,6) were assessed for mediation by entry into the regression after all other variables. SAS, version 8.2 (SAS Institute Inc., Cary, North Carolina) was used. Because a significant percentage of children with CE were in foster/adoptive care,(7) analyses of covariance (ANCOVA) evaluated differences between children in birth maternal/relative care, those in foster/adoptive care, and children with NCE.

RESULTS

Mothers with CE had less prenatal care, were older (~ 4 years), slightly less educated, and primarily unmarried with lower vocabulary scores (Table I). Infants with CE were exposed to more alcohol, marijuana, and tobacco prenatally, had lower birthweight, length, and head circumference, and were more likely preterm (Table II).

By 9 years, there were 11 child deaths, 8 children with CE and 3 children with NCE ($\chi^2 = 1.9$, $p < .17$), and 371 (192 CE, 179 NCE) children (92%) were assessed. 44 children with CE and 8 children with NCE ($\chi^2 = 26.2$, $p < .001$) were in adoptive/foster care. Caregiver and home environment characteristics did not differ except that caregivers of children with CE had lower vocabulary scores, and used more tobacco in the previous month. Of 33 children not seen, 18 children with CE were more likely to be white, of higher birthweight and head circumference, with lower Hobel risk scores and had mothers with lower WAIS-R picture completion scores than participants. The 15 children with NCE not seen had lower alcohol exposure, birth length, and Hobel risk scores and higher gestational age than the participants with NCE.

Groups did not differ in school grade placement, repeated grades, or special education. Children with CE were marginally more likely to receive a mental health service [58, (30.9%) vs. 40 (23%) $\chi^2 = 3.1$, $p < .08$]. 293 children (150 CE, 143 NCE) had blood levels determined.(4) Elevated lead exposure (≥ 10 mg/dl) was marginally lower for children with CE, 26 (17.3%) vs. 38 (26.6%) NCE ($\chi^2 = 3.6$, $p < .056$), and more children with CE (9 (4.69%) than NCE (2 (1.12%)), $\chi^2 = 4.1$, $p = 0.04$) had IDA.

Cocaine Effects

The MANOVA on the Domain IQ scores of the WISC-IV was significant (Wilks' $\lambda = 0.97$ [F = 2.46, df = 4,365, $p < .045$]) as was the MANCOVA on Perceptual Reasoning IQ (Wilks' $\lambda = 0.98$ [F = 2.65, df = 3,366, $p < .049$]). Children with CE had lower Perceptual Reasoning IQ's (M's = 87.6 ± 1 vs. 90.6 ± 1 , F = 3.9, df, 6,355, $p < .05$), and a higher percentage of children with significant deficits, (i.e. < 85 standard score), 81 (42% CE) vs. 58 (32% NCE), $\chi^2 = 3.9$, $p < .047$. Moreover, when classified into heavier and lighter exposure groups, there were greater effects with heavier exposure (Figure). There were no cocaine effects on the WJTOA.

The relative contributions of cocaine, other drugs, lead, IDA, and HOME environment are shown in Table III (available at www.jpeds.com). Significant cocaine effects became more pronounced once lead and IDA were controlled. CE was marginally related to a lower likelihood of achieving an IQ score above the normative mean. The concentration of benzoylecgonine was negatively related to Perceptual Reasoning IQ ($\beta = -.15$, SE = .26, $p < .$

03), and matrix reasoning ($\beta = -.17$, $SE = .05$, $p < .02$), and m-OH- benzoylecgonine was marginally related to matrix reasoning ($\beta = -.11$, $SE = .06$, $p < .10$). Cocaine effects on Perceptual Reasoning IQ were mediated by lower head circumference at birth.

Other Effects

Alcohol exposure predicted poorer Working Memory IQ, vocabulary and marginally lower Full Scale IQ. Adverse lead effects were detectable on Verbal Comprehension, Perceptual Reasoning and Full Scale IQ; academic achievement; and a lower likelihood of an IQ above the mean. IDA was associated with lower scores on similarities, math and marginally to poorer reading skills. Marijuana exposure was related to poorer performance on coding, which measures processing speed.

The quality of the home environment and birth mother vocabulary predicted multiple outcomes, including Verbal Comprehension IQ, similarities, vocabulary, Perceptual Reasoning IQ and its subscales, Working Memory, Processing Speed, and Full Scale IQ's, (all p 's $< .05$). Lower maternal parity at the study child's birth predicted higher Verbal Comprehension IQ ($p < .05$), as did the current caregiver's alcohol use ($p < .05$). Caregiver WAIS-R block design score predicted child score ($p < .05$) and birth mother psychological distress at childbirth marginally ($p < .10$) predicted Matrix reasoning. There were no moderating effects of sex or race.

Placement Effects

Children with CE in foster/adoptive care had caregivers with better vocabulary and less psychological distress than those in maternal/relative care (Table IV). Lead exposure was also lower, but they had almost twice the level of prenatal cocaine exposure. Children with CE in foster/adoptive care were less likely to achieve an IQ > 100 (the normative mean) than the group with NCE (adjusted O.R. = .11 [95% C.I., 0.01–0.89], $p < .039$). Only one child with CE in foster/adoptive care attained an IQ score > 100 . There was no difference in mean IQ or in the incidence of mental retardation.

CONCLUSIONS

This study relates specific cognitive deficits at school age to prenatal cocaine exposure in a large sample of children with a high follow-up rate, controlled for confounding drug, alcohol, environmental factors, and corroboration of exposure biomarkers. Perceptual reasoning skills were adversely affected, reflecting impairments in fluid reasoning and abstract categorical reasoning.(22,23) Brain imaging studies(23,24) indicate less mature development of frontal white matter pathways, and smaller volumes of the corpus callosum and parietal lobes in children with CE which may underlie these deficits. Effects were mediated by smaller birth head circumference, which has been found to be affected by prenatal CE in human(5,6) and nonhuman primate studies.(2) Birth head circumference may serve as an early marker of brain growth impairment and cognitive deficits in children with CE. Although school achievement appeared unaffected by cocaine, at 9 years, academic skills may not require significant perceptual abstraction skills, or alternatively, tests may not have been sensitive to drug effects.

Lead exposure had additive effects on multiple outcomes indicating continued risk to poor urban children despite screening programs.(25) Children with CE in foster/adoptive care had lower lead exposure.(26) The high rate of elevated lead levels in children in birth maternal/relative care confirms lead remains a major problem for poor urban children.(27) Discrete effects of alcohol exposure were discernible on Working Memory IQ, also noted in a NCE sample at 7 1/2 years of age,(28) and on verbal learning, as seen in a study of 10 year old children.(29) IDA was related to poorer verbal abstraction, perceptual-motor and math skills,

consistent with studies of non-U.S. iron deficient children.(30,31) Marijuana exposure affected perceptual-motor processing consistent with visual-cognitive deficits in adolescents with prenatal marijuana exposure.(32)

The present findings demonstrate the necessity of documenting all postnatal environment aspects that may affect development because more heavily cocaine-exposed children were placed with more educated, less distressed caregivers, and had lower lead and IDA than children in birth families. Without consideration of those factors, the negative effects of prenatal cocaine exposure may have been masked. The preventable nature of many of the risk factors associated with the cognitive deficits indicates significant need for drug and alcohol treatment of pregnant women, and pediatric surveillance for IDA as prenatal exposure to cocaine and alcohol may lead to increased IDA.(4,33) The most pervasive negative effects were associated with lead, highlighting the need for stronger public health efforts. The positive impact of a better caregiving environment supports the need for early intervention for infants with CE.

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Figure 1.

Perceptual reasoning IQ by level of cocaine exposure ($F=3.97$, $df=9, 264$, $p=.02$) with significant post-hoc mean difference between No cocaine group and Heavier cocaine exposed group ($p=.0207$). The heavier cocaine group was determined by benzoylecgonine meconium screen (≥ 216 nanograms/gm) or maternal self-report (≥ 17.5 units per week) indicating use greater than the 70th percentile for the cocaine users. The provided mean scores were adjusted for the HOME score, parity, maternal number of prenatal visits, biological maternal PPVT-R, psychological distress at birth, current caregiver's block design subscale of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) and lead level.

Maternal and Current Caregiver Characteristics by Prenatal Cocaine Exposure

Table 1

Biological Maternal	COCAINE (n = 192) n (%)		NON-COCAINE (n = 179) n (%)		χ^2	p
	Mean	(SD)	Mean	(SD)		
Race (non-white)						
Prenatal care	29.8	(5.0)	25.6	(4.8)	.34	.56
Married	3.5	(1.9)	2.7	(1.9)	7.8	.005
Low socioeconomic status	5.2	(4.6)	8.8	(4.9)	5.4	.02
Education < high school graduate	11.6	(1.7)	12.0	(1.4)	.01	.93
Drug Use During Pregnancy					7.5	.006
Alcohol						
Marijuana	11.5	(11.2)	4.0	(7.5)	20.4	<.0001
Tobacco	9.7	(17.5)	1.4	(4.6)	52.0	<.0001
Amphetamine*	1.3	(3.4)	0.6	(3.5)	88.0	<.0001
Barbiturate*	24.4	(45.8)	77.9	(14.8)	1.1	.45
Heroin*	73.8	(15.2)	7.1	(2.1)	.003	1.00
PCP*	6.9	(2.1)	7.0	(2.4)	3.7	.12
	.82	(.75)	.50	(.53)	9.45	.002
Age (years)	84.1	(9.8)	86.9	(10.3)		
Parity	6.9	(2.3)	7.1	(2.2)		
Number of prenatal visits	7.0	(2.4)	7.0	(2.4)		
education	.35	(.37)	.39	(.51)		
Amount of drug use during pregnancy						
Tobacco ^a	6.1	(7.7)	3.8	(6.5)		
Alcohol ^b	1.4	(3.1)	1.3	(3.9)		
Marijuana ^b	.30	(2.2)	.37	(2.1)		
PPVT-R score ¹						
WAIS-R BD score ²						
WAIS-R PC score ³						
General severity index						
Amount of drug use past 30 days						
Tobacco ^d						
Alcohol ^b						
Marijuana ^b						

* Based on Fisher exact test

** Unequal variance assumed

¹ Peabody Picture Vocabulary Test – Revised

² Wechsler Adult Intelligence Scale - Revised Block Design Score

³ Wechsler Adult Intelligence Scale - Revised Picture Completion Score

⁴ Home Observation for Measurement of the Environment

[†] Primary female caregiver to child at 9 years of age

^a Mean number of cigarettes per day

^b Mean number of drinks, "joints," or "rocks"/day $\times$ mean number of days/week

Table 2

Child Characteristics

	COCAINE (n = 192)		NON-COCAINE (n = 179)		χ^2	p
	n (%)		n (%)			
Sex (male)	87 (45.3)		87 (48.6)		.4	.53
Prematurity (<37 weeks gestational age)	55 (28.7)		35 (19.6)		4.2	.04
Low birth weight (< 2500gms)	70 (36.5)		33 (18.4)		15.0	.0001
Very low birth weight (< 1500gms) *	12 (6.3)		7 (3.9)		1.04	.31
Small for gestational age	24 (12.7)		3 (1.7)		16.3	.0001
IDA	9 (4.7)		2 (1.1)		4.1	.04
	Mean	(SD)	Mean	(SD)	t/E	df
Gestational age (weeks)	37.8	(2.8)	38.4	(2.9)	2.23	369
Birth weight (grams)	2704	(645.0)	3101	(701.3)	39.2	2,368
Birth length (cm)	47.3	(3.9)	49.1	(3.7)	19.9	2,368
Head circumference (cm)	32.2	(2.1)	33.5	(2.4)	28.1	2,365
Hobel neonatal risk score	7.5	(16.5)	5.9	(15.9)	-0.92	364
Lead exposure at 2 and 4 years	6.98	(4.11)	8.10	(4.59)	2.28	291
Age at assessment	9.10 (0.24)		9.10 (0.20)		0.13	1,369

* Groups were matched for very low birth weight

Table 3
Adjusted Effects of Drug, Alcohol, IDA, and Lead Exposures on Child Outcomes (n = 293) *

WISC-IV Subscale	Cocaine	Prenatal Alcohol	Marijuana [†]	IDA	Postnatal Lead	HOME
Verbal Comprehension IQ				$\beta = -0.11, p < .07$	$\beta = -0.14, p < .02$	$\beta = -0.17, p < .004$
Similarities				$\beta = -0.12, p < .05$		$\beta = -0.18, p < .003$
Vocabulary		3 rd tri. $\beta = -0.12, p < .05$			$\beta = -0.18, p < .002$	$\beta = -0.13, p < .03$
Perceptual Reasoning IQ	$\beta = -0.16, p < .02$				$\beta = -0.16, p < .007$	$\beta = -0.15, p < .01$
Block design	$\beta = -0.17, p < .005$				$\beta = -0.12, p < .06$	
Picture concept	$\beta = -0.14, p < .03$					
Matrix reasoning	$\beta = -0.11, p < .07$				$\beta = -0.18, p < .003$	
Working Memory IQ		Average $\beta = -0.14, p < .04$				$\beta = 0.16, p < .01$
Digit span		3 rd tri. $\beta = -0.13, p < .04$		$\beta = -0.11, p < .07$	$\beta = -0.10, p < .09$	$\beta = 0.17, p < .004$
Letter-number sequencing		Average $\beta = -0.18, p < .007$				$\beta = 0.15, p < .02$
Process Speed IQ			3 rd tri. $\beta = -0.22, p < .0005$	$\beta = -0.11, p < .07$		
Coding						
Symbol search						$\beta = 0.11, p < .06$
Full-scale IQ					$\beta = -0.14, p < .02$	$\beta = 0.16, p < .007$
Full-scale IQ > 100	O.R. = .51 (0.24 - 1.11), $p < .09$	3 rd tri. $\beta = -0.11, p < .08$			O.R. = .43 (0.22 - 0.85), $p < .02$	O.R. = 1.07 (1.00 - 1.14), $p < .05$
Woodcock-Johnson Subscale						
Reading Summary Score		3 rd tri. $\beta = -0.17, p < .008$		$\beta = -0.10, p < .08$	$\beta = -0.15, p < .01$	$\beta = 0.14, p < .02$
Letter-word					$\beta = -0.15, p < .01$	$\beta = 0.13, p < .03$
Identification Passage comprehension					$\beta = -0.18, p < .003$	$\beta = 0.10, p < .08$
Reading fluency				$\beta = -0.12, p < .04$	$\beta = -0.15, p < .02$	$\beta = 0.11, p < .07$
Math Summary Score				$\beta = -0.12, p < .04$		
Calculation				$\beta = -0.12, p < .04$		
Applied problems				$\beta = -0.10, p < .10$	$\beta = -0.12, p < .04$	
Math fluency				$\beta = -0.11, p < .07$		$\beta = 0.15, p < .02$

* Since the impact of combined cocaine- adoptive/ foster care effect was mediated completely by lead exposure, the β 's were estimated based on the model without the combined cocaine- adoptive/ foster care variable.

[†] There were several positive correlations of first trimester marijuana exposure on outcomes (β 's = .13, p 's < .05 for similarities, vocabulary, and picture concepts). However, since only 1 child was exposed only to marijuana during the first trimester, these were deleted.

Table 4
Comparisons of Key Environmental Characteristics and Child Outcomes by Caregiver Group

	COCAINE		NONCOCAINE		F/ χ^2	df	p
	Group I Birth Maternal/ Relative (n = 148) Mean (SD)	Group II Foster/Adoptive (n = 44) Mean (SD)	Group III (n = 179) Mean (SD)				
Prenatal cocaine exposure [*]	20.4 (35.7)	37.9 (68.8)	-----	3.7	1,190	.057	
Environmental							
HOME score	42.8 (5.7)	44.3 (4.9)	43.8 (6.2)	1.5	2,360	.23	
PPVT-R score	82.9 (7.8)	88.4(14.2)	86.9 (10.3)	8.4	2,357	.0003 ^a	
General Severity Index	.38 (.38)	.25 (.29)	.39 (.51)	2.8	2,351	.06 ^b	
Lead level ^{**}	7.3 (4.2)	5.6 (3.6)	8.1 (4.6)	5.6	2,290	.0004 ^c	
Lead level > 10 µg/dL at either 2 or 4 years ^{**}	31 (25.4%)	3 (10.7%)	44 (30.8%)	5.0		.08 ^d	
IDA [†]	8 (5.4%)	1 (2.3%)	2 (1.1%)	5.3		.08 ^e	
<i>Child outcomes</i>							
Full-scale IQ, Adjusted mean (SE) ^{***}	85.0 (1.1)	86.7 (2.1)	85.4 (1.0)	0.3	7,341	.78	
Full-scale IQ > 100	20 (13.5%)	1 (2.3%)	34 (19.0%)	8.2		.017 ^f	
Full-scale IQ < 70	16 (10.8%)	4 (9.1%)	16 (8.9%)	0.3		.84	
Perceptual Reasoning IQ < 70	18 (12.2%)	2 (4.7%)	11 (6.2%)	4.7		.095 ^g	

^{*} Mean number of "rocks"/day $\times$ mean number of days/week

^{**} Based on reduced sample size; n's are 118 for Group I, 32 for Group II, & 143 for Group III

^{***} Adjusted for the HOME score, parity, number of prenatal visits, biological maternal PPVT-R at birth, and average alcohol use during the 3rd trimester.

[†] Fisher exact test

^a Group I differs from Group II (p < .007) and from Group III (p < .002)

^b Group II differs from Group I (p < .04)

^c Group II differs from Group I (p < .05) and from Group III (p < .003)

^d Group II differs from Group III (p < .03)

^e Group I differs from Group III (p < .05)

^f Group II differs from Group III (p < .01)

^g Group I differs from Group III (p < .06)