Prenatal Cocaine Exposure: Drug and Environmental Effects at 9 Years

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Objective To assess school-age cognitive and achievement outcomes in children with prenatal cocaine exposure, controlling for confounding drug and environmental factors.

Study design At age 9 years, 371 children (192 cocaine exposure [CE]; 179 non–cocaine 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, blood lead level, iron-deficiency anemia (IDA), and foster/adoptive care.

Results Prenatal cocaine exposure predicted poorer perceptual reasoning IQ, with a linear relationship of the concentration of the cocaine metabolite benzoylecgonine to the 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 the home environment were additive. The CE children in foster/adoptive care had better home environments and lower lead levels. School achievement was not affected.

Conclusions Persistent teratologic effects of CE on specific cognitive functions and additive effects of alcohol, lead, and marijuana exposure; IDA; and the home environment were identified. Documenting environmental factors in behavioral teratology studies is important, because in this sample, CE was associated with better home environment and lower environmental risk in a substantial number of children. *(J Pediatr 2008;153:105-11)*

Hundreds of thousands of children exposed prenatally 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 cocaine 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] Conducting human studies is more difficult because of variability in timing, dose, and duration of exposure, as well as numerous confounding factors, including low socioeconomic status; maternal psychological distress, lower IQ, and low education level; polydrug exposure; poor prenatal care; iron-deficiency anemia (IDA); and lead exposure.[4] Out-of-home placement is common, and there often is significant, selective attrition in longitudinal studies.

Recent large, well-controlled studies with high retention rates have demonstrated negative effects of prenatal cocaine exposure on fetal growth, birth weight, 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 on children at school age, when earlier problems may resolve or may become more pronounced in response to greater cognitive demands, and the 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 cocaine exposure, controlling for confounding factors.

CE	Cocaine exposure	OR	Odds ratio
CI	Confidence interval	PPVT-R	Peabody Picture Vocabulary Scale–Revised
df	Degrees of freedom	SE	Standard error
Hb	Hemoglobin	SF	Serum ferritin
HOME	Home Observation of the Environment	TS	Transferrin saturation
IDA	Iron-deficiency anemia	WAIS-R	Wechsler Adult Intelligence Scale–Revised
MANCOVA	Multivariate analysis of covariance	WISC-IV	Wechsler Intelligence Scale for Children–Fourth Edition
MANOVA	Multivariate analyses of variance		
MCV	Mean corpuscular volume	WJTOA-III	Woodcock-Johnson–III Tests of Achievement
NCE	Non–cocaine exposure		

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METHODS

Subjects

The study subjects included 9-year-old children enrolled in a longitudinal study from birth (September 1994 to 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 involvement with the Department of Human Services, or self-admitted use underwent toxicology screening. 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, CA), followed by 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; US Drug Testing Laboratories, Inc, Des Plaines, IL). Cutoff levels were as follows: cocaine and metabolites, 25 ng/g; opiates, 25 ng/g; amphetamines, 100 ng/g; phencyclidine, 25 ng/g; tetrahydrocannabinol, 25 ng/g. Confirmatory assays were conducted. Specificity for both urine and meconium cutoffs was 99%.

An infant was placed in the cocaine exposure (CE) group if the mother reported use during pregnancy or if her urine or her infant's urine or meconium were positive, or in the non–cocaine exposure (NCE) group if maternal self-report, urine, and meconium assays were all negative. Of the 647 mothers and infants identified, 54 were excluded (20 CE, 34 NCE)—15 for no meconium, 2 due to Down syndrome, 16 due to maternal psychiatric history, 2 due to primary heroin use, 5 because of positive human immunodeficiency virus status, 1 due to maternal IQ $<$ 70, 1 due to fetal alcohol syndrome, 2 due to maternal age under 19 years, 3 due to a medical illness in the infant, 4 due to chronic illness in the mother, and 3 for other reasons. A total of 155 women (49 CE, 106 NCE) refused to participate; 23 (9 CE, 14 NCE) did not come to the enrollment visit. Consequently, a total of 415 women and infants (218 CE, 197 NCE) were enrolled.

Approval for human research was received from the Institutional Review Boards of MetroHealth Medical Center and University Hospitals of Cleveland. Compliance with the Health Insurance Portability & Accountability Act of 1996 (HIPPA) was maintained. Written consent was obtained from the parent/guardian of each subject and, when appropriate, from the subject himself or herself. All subjects were protected by a writ of confidentiality (DA-04-03) which prevents the principal investigator from being forced to reveal any subject information from the research, even under court order.

Procedures

After birth, a research assistant interviewed each mother about prenatal drug use.[13] To quantify use, the mother was asked to recall frequency and amount for the month before pregnancy and for each trimester of pregnancy. The number of tobacco cigarettes and marijuana "joints" smoked per day and the number of drinks of beer, wine, or hard liquor consumed per day (with each drink equivalent to 0.5 oz of absolute alcohol) were computed. 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 that a drug was used, except for cigarettes, which was recorded as the number smoked per day. Frequency was multiplied by the amount used per day to compute an average use score for the month before 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 not) were determined. The Peabody Picture Vocabulary Scale–Revised (PPVT-R),[14] and the block design and picture completion subscales of the Wechsler Adult Intelligence Scale–Revised (WAIS-R)[15] were used to obtain measures of maternal vocabulary and nonverbal intelligence. The General Severity Index, a summary scale of the Brief Symptom Inventory,[16] was used to measure psychological distress. Maternal race, age, parity, and number of prenatal visits and infant gestational age, birth weight, length, head circumference, and Apgar scores were obtained from hospital records. The Hobel neonatal risk score[17] was used to assess neonatal risk.

At age 2 and 4 years, all 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 illness, or logistic difficulties. The numbers of subjects with valid blood measurements at 2 and 4 years were 143 and 274, respectively. For the 122 children with blood measurements at both times, the values were averaged. A greater percentage of African-American and married women and a lower percentage of foster parents consented to blood collection. Elevated blood lead values were defined as $\geq$10 mg/dL at either 2 or 4 years.

Hematologic assessments included hemoglobin (Hb), mean corpuscular volume (MCV), percent 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 previous studies[18,19] for cutoff values at 2 years (Hb $<$ 11.0 g/dL; MCV, 70 m^3, TS, 10%; SF, 12 g/L); and at 4 years (Hb $<$ 11.2 g/dL, MCV, 73 m^3; TS, 12%; SF, 12 g/L).

At age 9 years, examiners unaware of the children's cocaine exposure 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 assess math, reading, and written lan-

guage ability. The WISC-IV yields a full-scale and 4 summary IQ scores (verbal comprehension, perceptual reasoning, processing speed, and working memory). The elementary school version of the Home Observation of the Environment (HOME)[21] was administered 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

The statistical analyses were conducted 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 $P < .10$. The order of entry was as follows: HOME; maternal age, parity, and number of prenatal care visits; maternal years of education, marital status, and socioeconomic status; birth mother and current caregiver PPVT-R and WAIS-R block design and picture completion scores, foster/adoptive care status, birth mother and current caregiver psychological distress, and prenatal and concurrent cigarette, alcohol, marijuana, and cocaine exposure. Sex and race did not differ by cocaine exposure 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, in the 271 children with available 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, NC) was used. Because a significant percentage of the CE children were in foster/adoptive care,[7] multivariate analysis of covariance (MANCOVA) was used to evaluate differences among children in birth maternal/relative care, those in foster/adoptive care, and NCE children.

RESULTS

The mothers of CE infants had less prenatal care; were older (~4 years), slightly less educated, and primarily unmarried; and had lower vocabulary scores (Table I). The CE infants were exposed to more alcohol, marijuana, and tobacco prenatally; had lower birth weight, length, and head circumference; and were more likely preterm (Table II).

By age 9 years, 11 of the children in the study group (8 CE and 3 NCE; $\chi^2 = 1.9$; $P < .17$) had died; 371 children (192 CE, 179 NCE) (92%) were assessed. A total of 52 children (44 CE and 8 NCE; $\chi^2 = 26.2$; $P < .001$) were in adoptive/foster care. Caregiver and home environment characteristics did not differ except that caregivers of the CE children had lower vocabulary scores and used more tobacco in the previous month. Of the 33 children not seen, the 18 CE children were more likely to be Caucasian; to have had higher birth weight, greater head circumference, and lower Hobel risk scores; and to have mothers with lower WAIS-R picture completion scores compared with the study participants, and the 15 NCE children had lower alcohol exposure, birth length, and Hobel risk scores and greater gestational age compared with the participants.

The 2 groups did not differ in terms of school grade placement, repeated grades, or special education. The CE children were marginally more likely to receive a mental health service (58 [30.9%] vs 40 [23%]; $\chi^2 = 3.1$; $P < .08$). A total of 293 children (150 CE, 143 NCE) had blood levels determined.[4] Elevated lead exposure (≥10 mg/dL) was marginally lower in the CE children (26 [17.3%] vs 38 [26.6%]; $\chi^2 = 3.6$; $P < .056$), and more CE children had IDA (9 [4.69%] vs 2 [1.12%]; $\chi^2 = 4.1$; $P = .04$).

Cocaine Effects

MANOVA on the domain IQ scores of the WISC-IV was significant (Wilks' $\lambda = 0.97$ [$F = 2.46$; degrees of freedom (df) = 4.365; $P < .045$]), as was MANCOVA on perceptual reasoning IQ (Wilks' $\lambda = 0.98$ [$F = 2.65$; df = 3,366; $P < .049$]). The CE children had lower perceptual reasoning IQ ($M = 87.6 \pm 1$ vs 90.6 ± 1; $F = 3.9$; df = 6,355; $P < .05$) and a higher percentage of significant deficits (<85 standard score: CE, 81 (42%) vs NCE, 58 (32%); $\chi^2 = 3.9$l; $P < .047$). Moreover, when the CE children were classified into heavier and lighter exposure groups, greater effects were seen in the heavier exposure group (Figure). No association was found between cocaine exposure and WJTOA-III score.

The relative contributions of cocaine, other drugs, lead, IDA, and HOME environment are given in Table III (available at www.jpeds.com). Significant cocaine effects became more pronounced once lead and IDA were controlled. Cocaine exposure 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 ($\beta = -0.15$; standard error [SE] = 0.26; $P < .03$), and matrix reasoning ($\beta = -0.17$; SE = 0.05; $P < .02$), and m-OH-benzoylecgonine was marginally related to matrix reasoning ($\beta = -0.11$; SE = 0.06; $P < .10$). The effects of cocaine exposure on perceptual reasoning IQ were mediated by smaller head circumference at birth.

Other Effects

Alcohol exposure predicted poorer working memory IQ and vocabulary and marginally lower full-scale IQ. Adverse effects of lead exposure 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 and

Table I. Maternal and current caregiver characteristics by prenatal cocaine exposure

	CE (n = 192), n (%)	NCE (n = 179), n (%)	χ^2	P
Biological maternal				
Race (non-Caucasian)	160 (83.3)	145 (81.0)	.34	.56
Prenatal care	154 (80.2)	162 (90.5)	7.8	.005
Married	16 (8.3)	29 (16.2)	5.4	.02
Low socioeconomic status	187 (97.9)	175 (97.8)	.01	.93
Education, less than high school graduate	90 (46.9)	59 (33.0)	7.5	.006
Drug use during pregnancy				
Alcohol	160 (86.0)	113 (65.7)	20.4	<.0001
Marijuana	91 (48.9)	23 (13.4)	52.0	<.0001
Tobacco	162 (87.1)	68 (39.5)	88.0	<.0001
Amphetamines*	5 (2.7)	2 (1.2)	1.1	.45
Barbiturates*	1 (.54)	1 (.58)	.003	1.00
Heroin*	4 (2.2)	0 (0)	3.7	.12
PCP*	10 (5.5)	0 (0)	9.45	.002
	Mean (SD)	**Mean (SD)**	**t**	**df**	
Age (years)	29.8 (5.0)	25.6 (4.8)	−8.3	369	.0001
Parity	3.5 (1.9)	2.7 (1.9)	−4.2	369	.0001
Number of prenatal visits	5.2 (4.6)	8.8 (4.9)	7.2	368	.0001
Maternal education†	11.6 (1.7)	12.0 (1.4)	2.24	365	.026
Amount of drug use during pregnancy					
Tobacco‡	11.5 (11.2)	4.0 (7.5)	−10.5	355	.0001
Alcohol†,§	9.7 (17.5)	1.4 (4.6)	−10.5	299	.0001
Marijuana†,§	1.3 (3.4)	0.6 (3.5)	−4.2	330	.0001
Cocaine§	24.4 (45.8)				
PPVT-R score	73.8 (15.2)	77.9 (14.8)	2.6	367	.01
WAIS-R BD score¶	6.9 (2.1)	7.1 (2.1)	1.0	359	.31
WAIS-R PC score**	6.7 (2.1)	7.0 (2.4)	0.99	359	.32
General Severity Index†	0.82 (0.75)	0.50 (0.53)	−5.4	366	.0001
Caregiver at age 9 years††					
PPVT-R score	84.1 (9.8)	86.9 (10.3)	2.7	358	.008
WAIS-R BD score¶	6.9 (2.3)	7.1 (2.2)	1.0	345	.32
WAIS-R PC score**	7.0 (2.4)	7.0 (2.4)	−0.09	345	.93
General Severity Index†	0.35 (0.37)	0.39 (0.51)	−0.58	342	.56
Amount of drug use in the previous 30 days					
Tobacco‡	6.1 (7.7)	3.8 (6.5)	−3.7	349	.0003
Alcohol§	1.4 (3.1)	1.3 (3.9)	−0.3	350	.73
Marijuana§	0.30 (2.2)	0.37 (2.1)	−0.26	348	.80

*Based on Fisher exact test.
†Unequal variance assumed.
‡Mean number of cigarettes smoked per day.
§Mean number of drinks, "joints," or "rocks"/day times mean number of days/week.
¶WAIS-R Block Design Score.
**WAIS-R Picture Completion Score.
††Primary female caregiver to the child at age 9 years.

math and marginally 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's vocabulary predicted multiple outcomes, including verbal comprehension IQ, similarities, vocabulary, perceptual reasoning IQ and its subscales, working memory IQ, processing speed IQ, and full-scale IQ (all $P < .05$). Lower maternal parity at the 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 the child's score ($P < .05$), and the birth mother's psychological distress at childbirth marginally ($P < .10$) predicted matrix reasoning. There were no moderating effects of sex or race.

Placement Effects

The CE children in foster/adoptive care had caregivers with a better vocabulary and less psychological distress compared with those in maternal/relative care (Table IV). They also had lower lead exposure, but almost twice the level of prenatal cocaine exposure. CE children in foster/adoptive care were less likely to achieve an IQ score >100 (the normative mean) compared with NCE children (adjusted odds ratio

Table II. Child characteristics

	CE (n = 192), n (%)	NCE (n = 179), n (%)	χ^2	P
Male sex	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 (<2500 g)	70 (36.5)	33 (18.4)	15.0	.0001
Very low birth weight (<1500 g)*	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/F**	**df**
Gestational age, weeks	37.8 (2.8)	38.4 (2.9)	2.23	369 .03
Birth weight, g	2704 (645.0)	3101 (701.3)	39.2	2,368 .0001
Birth length, cm	47.3 (3.9)	49.1 (3.7)	19.9	2,368 .0001
Head circumference, cm	32.2 (2.1)	33.5 (2.4)	28.1	2,365 .0001
Hobel neonatal risk score	7.5 (16.5)	5.9 (15.9)	−0.92	364 .36
Lead exposure at 2 and 4 years	6.98 (4.11)	8.10 (4.59)	2.28	291 .02
Age at assessment, years	9.10 (0.24)	9.10 (0.20)	0.13	1,369 .72

*Groups were matched for very low birth weight.

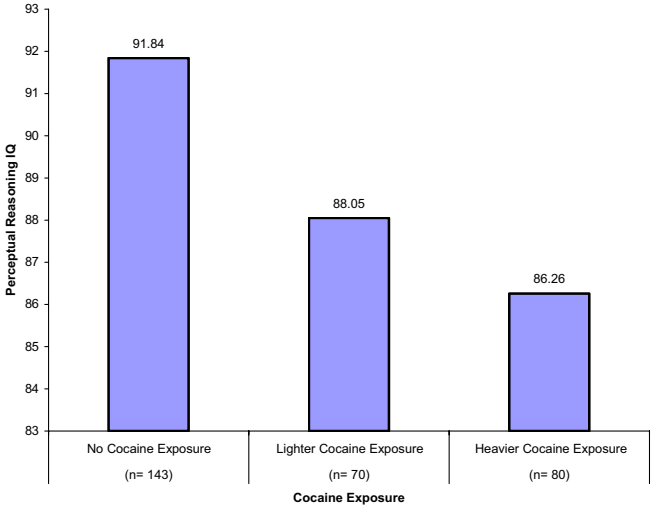

Figure. Perceptual reasoning IQ by level of cocaine exposure ($F = 3.97$; df = 9,264; $P = .02$) with significant post hoc mean difference between the NCE group and the heavier CE group ($P = .0207$). The heavier CE group was determined by benzoylecgonine meconium screening (≥216 ng/g) or maternal self-report (≥17.5 units/week) indicating use >70th percentile for cocaine users. The provided mean scores were adjusted for HOME score, parity, maternal number of prenatal visits, biological maternal PPVT-R, psychological distress at birth, current caregiver's block design subscale of the WAIS-R, and lead level.

[OR] = 0.11; 95% confidence interval [CI] = 0.01 to 0.89; $P < .039$). Only 1 CE child in foster/adoptive care attained an IQ score >100. There was no difference in mean IQ or in the incidence of mental retardation between the CE and NCE groups.

DISCUSSION

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, controlling for confounding drug, alcohol, and environmental factors and corroboration of exposure biomarkers. In the CE children, 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 prenatal cocaine exposure, which may underlie these deficits. Effects were mediated by smaller birth head circumference, which has been linked to prenatal cocaine exposure in both 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 prenatal cocaine exposure. Although school achievement appears to be unaffected by cocaine exposure, at age 9 years, academic skills may not require significant perceptual abstraction skills, or, alternatively, the tests may not be sufficiently sensitive to drug effects.

Lead exposure had additive effects on multiple outcomes, indicating continued risk to poor urban children despite screening programs.[25] The CE children in foster/adoptive care had lower levels of lead exposure.[26] The high prevalence of elevated lead levels in children in birth maternal/relative care confirms that lead remains a major problem for poor urban children.[27] Discrete effects of alcohol exposure were discernible on working memory IQ, as also was noted in a sample of NCE children at age 7-1/2 years,[28] and on verbal learning, as was 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–US iron-deficient children.[30,31] Marijuana exposure affected perceptual-motor processing, consistent with visual-cognitive deficits found in adolescents with prenatal marijuana exposure.[32]

Our findings demonstrate the necessity of documenting all postnatal environment aspects that may affect development, because the more heavily cocaine-exposed CE children

Table IV. Comparisons of key environmental characteristics and child outcomes by caregiver group

	CE		NCE			
	Group I, birth mother/relative (n = 148), mean (SD)	Group II, foster/adoptive (n = 44), mean (SD)	Group III (n = 179), mean (SD)	F/χ^2	df	P
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¶
General Severity Index	0.38 (.38)	0.25 (.29)	0.39 (.51)	2.8	2,351	.06**
Lead level†	7.3 (4.2)	5.6 (3.6)	8.1 (4.6)	5.6	2,290	.0004††
Lead level ≥10 g/dL at either 2 or 4 years†	31 (25.4%)	3 (10.7%)	44 (30.8%)	5.0		.08‡‡
IDA‡	8 (5.4%)	1 (2.3%)	2 (1.1%)	5.3		.08§§
Child outcomes						
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¶¶
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***

SD, standard deviation.
*Mean number of "rocks"/day times mean number of days/week.
†Based on reduced sample size; n = 118 for group I, 32 for group II, and 143 for group III.
‡Fisher exact test.
§Adjusted for HOME score, parity, number of prenatal visits, biological maternal PPVT-R at birth, and average alcohol use during the third trimester.
¶Group I differs from group II ($P < .007$) and from group III ($P < .002$).
**Group II differs from group I ($P < .04$).
††Group II differs from group I ($P < .05$) and from group III ($P < .003$).
‡‡Group II differs from group III ($P < .03$).
§§Group I differs from group III ($P < .05$).
¶¶Group II differs from group III ($P < .01$).
***Group I differs from group III ($P < .06$).

were placed with more-educated, less-distressed caregivers, and they had lower lead levels and rate of IDA compared with the CE children in birth families. Had these factors not been considered, 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 demonstrates the importance of drug and alcohol treatment in pregnant women and pediatric surveillance for IDA, because prenatal exposure to cocaine and alcohol may lead to increased IDA.[4,33] The most pervasive negative effects were associated with lead exposure, underscoring the need for stronger public health efforts. The positive impact of a better caregiving environment supports the need for early intervention for infants with prenatal cocaine exposure.

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Table III. Adjusted effects of prenatal drug and alcohol exposure and postnatal IDA, lead exposure, and HOME score on child outcomes (n = 293)*

	Prenatal			Postnatal		
	Cocaine	Alcohol	Marijuana†	IDA	Lead	HOME
WISC-IV Subscale						
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		Third trimester, $\beta = -0.12$; $P < .05$			$\beta = -0.18$; $P < .002$	$\beta = 0.13$; $P < .03$
Comprehension						$\beta = 0.15$; $P < .01$
Perceptual reasoning IQ	$\beta = -0.16$; $P < .02$				$\beta = -0.16$; $P < .007$	
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		Third trimester, $\beta = -0.13$; $P < .04$			$\beta = -0.10$; $P < .09$	
Letter-number sequencing		Average, $\beta = -0.18$; $P < .007$		$\beta = -0.11$; $P < .07$		$\beta = 0.17$; $P < .004$
Processing speed IQ						$\beta = 0.15$; $P < .02$
Coding			Third trimester, $\beta = -0.22$; $P < .0005$	$\beta = -0.11$; $P < .07$		
Symbol search						$\beta = 0.11$; $P < .06$
Full-scale IQ		Third trimester, $\beta = -0.11$; $P < .08$			$\beta = -0.14$; $P < .02$	$\beta = 0.16$; $P < .007$
Full-scale IQ >100	OR = 0.51 (95% CI = 0.24 to 1.11); $P < .09$				OR = 0.43 (95% CI = 0.22 to 0.85); $P < .02$	OR = 1.07 (95% CI = 1.00 to 1.14); $P < .05$
Woodcock-Johnson subscale						
Reading summary score		Third trimester, $\beta = -0.17$; $P < .008$		$\beta = -0.10$; $P < .08$	$\beta = -0.15$; $P < .01$	$\beta = 0.14$; $P < .02$
Letter-word identification					$\beta = -0.15$; $P < .01$	$\beta = 0.13$; $P < .03$
Passage comprehension					$\beta = -0.18$; $P < .003$	$\beta = 0.10$; $P < .08$
Reading fluency					$\beta = -0.15$; $P < .02$	$\beta = 0.11$; $P < .07$
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				$\beta = -0.11$; $P < .07$		$\beta = 0.15$; $P < .02$

*Because the impact of combined cocaine exposure and adoptive/foster care effect was mediated completely by lead exposure, the β values were estimated based on the model without the combined cocaine exposure and adoptive/foster care variable.

†There were several positive correlations of first-trimester marijuana exposure on outcomes ($\beta = 0.13$; $P < .05$) for similarities, vocabulary, and picture concepts); however, because only 1 child was exposed only to marijuana during the first trimester, these were deleted.