

# Outcome from a Prospective, Longitudinal Study of Prenatal Cocaine Use: Preschool Development at 3 Years of Age

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**Objective** To determine the effects of prenatal cocaine exposure on child development.

**Methods** This prospective, longitudinal study recruited 154 pregnant cocaine users who were matched on race, parity, socioeconomic status, and perinatal risk to 154 noncocaine users. Drug use status was determined by maternal history and urine screening. At 3 years of age, the child subjects were assessed by an evaluator blinded to maternal drug use history. During a home visit at age 3, caregiver, family, and home assessments were administered. **Results** Structural equation modeling showed a direct effect of the amount of prenatal cocaine exposure on the adjusted birth head circumference which in turn directly affected preschool development. **Conclusions** We could not demonstrate a direct effect of prenatal cocaine exposure on preschool development, a result that is consistent with that of earlier work and now extending findings to age 3. However, cocaine continued to exert an indirect effect on development through its direct effect on the head circumference at birth.

**Key words** prenatal cocaine use; preschool development; structural equation modeling.

The current cocaine epidemic has been in progress in this country since the early 1980s. With the ready availability and low cost of crack in the mid-1980s, its potency, increased potential for addiction, and frequent use by pregnant women gave rise to a new concern regarding potential affects on the developing fetus and child. Although a number of case reports, retrospective studies, and media articles heralded the dramatic effects of crack on a new generation of children, until more recently, no longitudinal, prospective studies were available to support or refute these initial concerns.

In 2001, Frank, Augustyn, Knight, Pell, and Zuckerman (2001) published a systematic review of the literature which included only studies that had enrolled prospectively, included a control group, and used evaluators blinded to drug group status. In addition, studies were excluded if subjects were exposed to opiates, other stimulants, and HIV. Of the 36 studies included in the review, only three reported psychomotor and cognitive

outcomes at 3 years of age, with two studies involving the same cohort. In two of the studies there were no cocaine effects on cognitive and psychomotor assessments at age 3 (Azuma & Chasnoff, 1993; Kilbride, Castor, Hoffman, & Fuger, 2000). However, Griffith et al. using the Stanford-Binet, demonstrated that children who had been cocaine-exposed had lower Verbal Reasoning scores than children who had not been exposed (Griffith, Azuma, & Chasnoff, 1994). At the time of the review only two groups had published studies of cognitive and psychomotor development in children beyond age 3 that met the criteria for inclusion in the review and none of the studies demonstrated cocaine effects on psychomotor development (Hurt et al., 1997, 1998; Richardson, Conroy, & Day, 1996).

Since that time, additional studies evaluating psychomotor development and cognition have been published. Bennett, Bendersky, and Lewis (2002) demonstrated a differential gender effect of prenatal cocaine exposure

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on outcome, with boys who had been exposed to cocaine, but not girls, having lower IQ scores at age four when compared with their counterparts who were not exposed. Using a prospective cohort of children, Hurt, Malmud, Betancourt, Brodsky, and Giannetta (2001) demonstrated lower developmental scores at ages three and five due to postnatal environmental factors, but not due to prenatal cocaine exposure.

Scientists, clinicians, and caregivers are all eager to know what to expect about the outcome of children who have been cocaine exposed. It is important that a body of data be available at pivotal developmental time points to understand the evolution of the effects of prenatal exposure on long-term outcome. Age 3, before children enter the environment of the public school system, is a pivotal time point and thus this article describes the caregivers, families, home environment, and the psychomotor development of the children themselves, at this important age.

We hypothesized that children who were cocaine exposed would score more poorly on developmental measures at age 3 than their matched controls who were not cocaine exposed. In addition, we hypothesized that compared with the children who were not exposed, the psychosocial status of the caregiver and the quality of the family support and home environment would be less optimal for those who had been cocaine-exposed. Thus, we have used structural equation modeling to describe both the direct and indirect effects of prenatal cocaine exposure on preschool development at age 3, taking into account pertinent caregiver and environmental effects as well as important biologic factors of the child.

## Methods

This study was approved by the Institutional Review Board of the University of Florida. A Certificate of Confidentiality from the National Institute on Drug Abuse, US Department of Health and Human Services (DA-91-45) protects the confidentiality of the research data collected. A project staff member approached all women for informed consent when they enrolled in prenatal care at the county public health department and were at least 15-weeks pregnant or in the case of little or no prenatal care, when they presented for delivery at our tertiary care center.

### Study Design

This is a longitudinal, prospective study of the medical and developmental effects of prenatal cocaine exposure which enrolled subjects from 1991 to 1993. Mothers

were recruited from a historically understudied population of rural public health department patients. A complete, detailed description of the longitudinal study has been published previously (Eyler, Behnke, Conlon, Woods, & Wobie, 1998). In summary, we prospectively enrolled prenatal cocaine users and a matched control group of noncocaine users when they first contacted the health care system for their pregnancy. This allowed us to minimize bias in participant enrollment and obtain the earliest drug history possible by enrolling subjects at either a prenatal clinic or the hospital in the case of no or limited prenatal care. We enrolled a sufficient sample size to allow for covariate analyses of possible confounding variables, and if necessary, to allow for an attrition rate of 33% over 3 years and still maintain needed statistical power to detect a significant difference of a third of a standard deviation between the exposed and nonexposed groups on measures of development. In addition, all assessments were made by appropriately trained, certified, or licensed professionals masked to study group membership of the mother and her child.

Subject matching criteria were chosen to minimize the effect on outcome of race, parity, socioeconomic status, and perinatal risk (that related to the location of prenatal care). Women were excluded a priori for the following reasons: (a) major illnesses that developed before pregnancy and were known to affect pregnancy outcome or developmental outcome of the fetus; (b) chronic use of prescription or over-the-counter drugs; (c) any illicit drug use other than marijuana and cocaine; (d) non-English-speaking; and (e) <18 years old. From over 2500 women who gave consent, were interviewed and not excluded, 154 were identified as cocaine users and continued in the longitudinal study. A pool of potential participants whose interviews and urine specimens indicated no evidence of prenatal cocaine use was maintained for each match category. As each target was identified, the longest held matched control was selected from the appropriate match category for study participation.

### Identification/Documentation of Drug Use

Drug use was identified in the sample using two different methods. Drug histories adapted from Day, Wagener, and Taylor (1985) were elicited from all women at the end of each trimester of pregnancy. Experienced interviewers privately asked about the amount, frequency, and pattern of *past* drug use, defined as drug use during the previous trimester of pregnancy, thought to provide more accurate data by being less threatening (Day et al., 1985; Jacobson et al., 1991). In an effort to maximize

the accuracy of subject classification, urine specimens were collected at two unanticipated times, study enrollment and at delivery. Urine screening included assessment for barbiturates, benzodiazepines, cocaine, marijuana, methamphetamines and amphetamines, opiates, phen-cyclidine, and propoxyphene using fluorescence polarization immunoassay (Mule & Casella, 1988). Cocaine was considered to be present when benzoylecgonine was detected at or above a cut-off of 300 ng/mL. All positive screens were confirmed using gas chromatography/mass spectrometry.

### 3-Year Evaluations

At 3 years of age, caregiver, family, and home assessments were performed in the child's home. In addition, a standardized caregiver report of the child was obtained. The child was assessed at a separate visit for the purpose of evaluating overall development. The caregiver, family, and home assessments chosen for use in this study have been shown to be associated with maternal drug use, as well as, either directly or theoretically to child outcome. The measures have been fully described in previous publications (Behnke, Eyler, Woods, Wobie, & Conlon, 1997; Bradley & Caldwell, 1976; Woods, Behnke, Eyler, Conlon, & Wobie, 1995)

Specific caregiver measures included the Center for Epidemiologic Studies-Depression (CES-D) (Radloff, 1977), Levenson Locus of Control (LOC) (Levenson, 1974), Parenting Sense of Competence (PSOC) (Gilbaud-Wallston, 1977), Rosenberg Self-esteem Scale (RSS) (Rosenberg, 1989), Concepts of Development Questionnaire (CODQ) (Sameroff & Feil, 1986), and Life Experiences Survey (LES) (Sarason, Johnson, & Siegel, 1978). The family evaluation included the Family Adaptability and Cohesion Evaluation Scales-III (FACES-III) (Edman, Cole, & Howard, 1990; Green, Harris, Forte, & Robinson, 1991; Olson, 1986; Olson, 1989) and the Family Support Scale (FSS) (Dunst, Jenkins, & Trivette, 1984). A home assessment was made using the Home Observation for Measurement of the Environment (HOME) (Bradley & Caldwell, 1976; Caldwell & Bradley, 1984). Caregiver report of the child's adaptive behavior was obtained using the Vineland Adaptive Behavior Scales (VABS) (Sparrow, Balla, & Cicchetti, 1984).

At a separate visit, an evaluation of the child was made by a licensed, experienced examiner blinded to maternal drug status. Assessments included the Mental (MDI) and Psychomotor (PDI) Developmental Indices of the Bayley Scales of Infant Development (Bayley, 1993).

### Statistical Analyses

Group comparisons for continuous data were made using the Wilcoxon Rank Sum and for categorical data using the Chi-square tests. Structural equation modeling (SEM) was used to test theoretical models that specify causal relationships between observed variables that were organized into meaningful constructs. Power analysis indicated that the sample size is sufficient for the number of degrees of freedom available in the SEM analyses reported in this article with power >0.80 (MacCallum, Browne, & Sugawara, 1996). Statistical significance for tests of hypotheses was set at 0.05.

After hypothesizing a theoretical model, specifying the relationships between constructs, and choosing indicator variables that operationalized the constructs, a two-step approach was followed. First, an acceptable measurement model was developed in which all constructs were allowed to correlate with each other. After verifying that the measurement model displayed an acceptable fit to the data, a structural model was developed by making modifications that specified the causal relationships between the latent constructs themselves.

To assess structural model fit, the indices recommended by Hoyle and Panter (1995) were used. The PROC CALIS procedure in SAS (SAS Institute, 1989) was chosen to perform all SEM path analyses. The maximum likelihood method was used to estimate free parameters. All models were estimated in covariance metric.

The model originally included eight constructs: amount of prenatal cocaine use, other prenatal substance use, adjusted birth head circumference, number of caregiver changes by age 3, caregiver problems at age 3, environmental factors at age 3, gender, and psychomotor development at age 3. Variables were considered a priori for inclusion in each construct based upon research theories, empirical data, and the constraints of the statistical methodology (Behnke et al., 1997; Behnke, Eyler, Garvan, Wobie, & Hou, 2002; Bradley & Caldwell, 1976; Woods et al., 1995). Ultimate variable selection was dependent upon significant factor loadings on the latent constructs as well as acceptable residual values to construct well-fitting measurement models (Hatcher, 1994). Previously established imputation methods were used to estimate missing data (Behnke et al., 2002) and accounted for <0.05% of the data available for any individual variable in the analysis.

Details concerning variable selection for each construct are as follows. A frequency measure of prenatal cocaine exposure was derived from the interview data to quantify the amount of cocaine exposure for the

Amount of Cocaine Use variable. The number of weeks that the mother reported using cocaine during the 12 weeks prior to pregnancy through the end of her pregnancy was divided by the total number of weeks of her pregnancy plus the 12 weeks prior to conception. Average daily use of tobacco (cigarettes smoked per day), alcohol (ounces of absolute alcohol per day) and marijuana (joints smoked per day) were considered for the Other Substance Use variable. Marijuana use did not have significant factor loading and was not retained in the model. On the basis of previous work from our group (Behnke et al., 2002), the Adjusted Birth Head Circumference variable included the head circumference as measured at birth, standardized across varying gestational ages. The Number of Caregiver Changes variable was a measure of the number of times the child changed caregivers during the first 3 years of life. This was thought to be a potentially important variable given the fact that 56% of the cocaine-exposed children ( $n = 77$ ) were not living with their biological mother compared to only 6% of the nonexposed children ( $n = 8$ ). The following measures were considered for inclusion in the variable Caregiver Problems: CES-D, LOC (Internal, Chance, and Powerful Others subscales), PSOC (Self-efficacy and Value of Parenting subscales), FSS (Number of Supports and Value of Supports subscales), and RSS. The LOC Internality subscale and the PSOC Self-efficacy subscale did not have significant factor loadings and were not retained in the model. Because the two FSS subscales did not load on the same factor as the other variables in the Caregiver Problems variable, a separate construct was developed entitled Family Support. For the Quality of the Environment variable, the following measures were considered for inclusion: the HOME (total score), LES (Balance subscale), and the CODQ (Categorical and Perspectivistic subscales). The LES Balance subscale and the CODQ Perspectivistic subscale were not retained in the model due to nonsignificant factor loadings. The Gender variable included male and female, which were assigned 1 and 0, respectively. The Bayley MDI and PDI and the Communication subscale and Motor Skills subscale of the VABS were included in the Preschool Development variable.

Data exhibiting skewness and high kurtosis were transformed prior to fitting of the measurement model. These included the Total HOME score, the amount of tobacco use, and the amount of alcohol use. The initial measurement model could not be fit. This was thought to be due to inclusion of the Number of Caregiver Changes and the Family Support latent constructs. These were eliminated and a measurement model was able to be fit to the data (see Table I).

Next, the theoretical structure model of hypothesized relationships between the latent variables represented in Figure 1 was tested. Model fit was improved by first eliminating nonsignificant paths one at a time (Bentler & Chou, 1987). The modification indices were inspected to determine whether there were any additional paths that needed to be estimated, and there were not. See Table I for fit statistics.

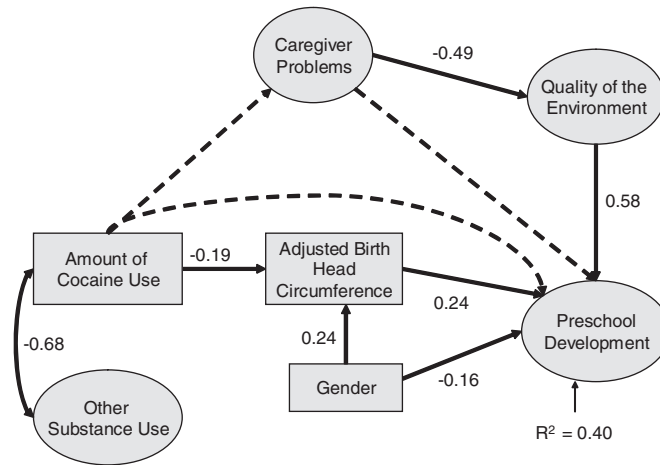
To quantify the magnitude of relationship between latent variables, all latent variables were set to the same unit of measurement (i.e., all latent variables were scaled to have a standard deviation of 1.00). This allowed the comparison of the relative sizes of standardized path coefficients to determine which independent variables had the largest effect on the dependent variable. The  $R^2$  value, which reflects the extent to which independent variables in the model account for variability in the dependent variable, was calculated for the Preschool Development outcome. Table II includes a list of parameter estimates and standard errors.

To interpret the results of the SEM, the loading of one indicator in each latent variable was constrained to unity (set to 1.00). This equates the scale of the latent variable with the scale of the constrained indicator variable. The indicator variables chosen to be constrained to unity were generally those with the highest loading on their factor and included amount of tobacco use for Other Substance Use, CES-D for Caregiver Problems, Total HOME score for Quality of the Environment, and MDI for Preschool Development. Owing to data transformations, the scale for the Other Substance Use latent variable is inversely proportional to tobacco use (a higher score represents less other drug use), the scale for the Caregiver Problems latent variable is the same as

**Table I.** Fit Statistics for the Measurement and Structural Equation Models

Model	$\chi^2$	df	p	GFI	RMSEA	CFI	NNFI	Comparison to measurement model		
								$\chi^2$	df	p
Measurement model	125.31	83	.0019	0.943	0.045	0.956	0.937	—	—	—
Structural equation model	140.05	96	.0023	0.936	0.043	0.955	0.943	14.74	13	.324

CFI = comparative fit index; GFI = goodness of fit index; NNF = nonnormed fit index; and RMSEA = root mean squared error of approximation.



**Figure 1.** SEM Analysis at Age 3 for Preschool Development Latent constructs are represented with ovals and manifest constructs with rectangles. Curved, double-headed arrows indicate constructs allowed to covary and single-headed arrows indicate directional pathways. Pathways that lacked statistical significance are indicated by dotted lines. Solid lines indicate significant pathways from the theoretical model.

**Table II.** Path Coefficients, Standard Errors, and *t* Values for the Structural Equation Model

	Unstandardized path coefficient	Standard error	<i>t</i> value	Standardized path coefficient
Adjusted birth head circumference				
Amount of cocaine use	-0.9290	0.2895	-3.2090	-0.1932
Gender	0.7210	0.1811	3.9813	0.2397
Quality of the environment				
Caregiver problems	-0.0441	0.0081	-5.4528	-0.4879
Preschool development				
Quality of the Environment	11.3346	2.2856	4.9592	0.5830
Adjusted birth head circumference	1.8017	0.5131	3.5114	0.2414
Gender	-3.4813	1.4971	-2.3254	-0.1551

that of the CES-D (a higher score represents more caregiver problems), the scale for the Quality of the Environment latent variable is the same as the Total HOME score (a higher score represents a higher quality environment), and the scale for the Preschool Development latent variable is the same as the Bayley MDI (a higher score represents better development).

**Results**

**Sample Description**

Of the original 308 subject pairs enrolled in the study, 10 children died (5 exposed and 5 nonexposed), and 22 children did not return for the 3-year visit (14 exposed and 8 nonexposed), leaving 276 caregivers and their offspring (a return rate of 92.6% of those still living at age 3). This included 135 children who had been cocaine exposed and 141 controls who were not cocaine exposed. The children were predominantly African-American (82% in both groups) and of low socioeconomic status (97%

in both groups). There was not a significant difference in the number of female children who had been cocaine-exposed and those who had not (52% vs. 44%; *p* = .1902) nor was there a significant difference in the age at evaluation (3.1 years in both groups).

**Caregiver, Family, and Home Assessments**

There were no significant group differences on the LOC, RSS, FACES-III, or seven of the eight HOME subscales. However, caregivers of the children who were cocaine exposed had significantly lower scores on the CES-D, Positive Events subscale of the LES, Balance (number of positive – number of negative events) subscale of the LES, Total score on the CODQ, and Number of Family Supports subscale of the FSS than the caregivers of the children who were not exposed. In addition, caregivers of children who were cocaine exposed had significantly higher scores on the Self-efficacy subscale of the PSOC and the Warmth and Acceptance subscale of the HOME. There were significantly more caregiver changes on average during

the first 3 years of life for the children who were cocaine exposed than for those who were not (see Table III).

### Child Assessments

There were no significant group differences on the MDI or PDI of the Bayley Scales of Infant Development. Nor were there any significant group differences on the Communication subscale and Motor Skills subscale of the VABS (see Table IV).

### Structural Equation Modeling

For the SEM analyses, 251 subjects had complete data for all the indicator variables included in the Preschool Development latent variable. Figure 1 represents the final model developed.

As seen in Figure 1, the amount of prenatal cocaine use was significantly correlated with other substance use during pregnancy (correlation coefficient =  $-0.68$ ). Gender significantly predicted both adjusted birth head

**Table III.** Caregiver, Family, and Home Assessments

	Cocaine-exposed		Nonexposed	
	<i>M</i> ± <i>SD</i>	<i>Mdn</i>	<i>M</i> ± <i>SD</i>	<i>Mdn</i>
Depression (CES-D)-total score <sup>a</sup>	20.0 ± 10.6	20.0*	22.2 ± 9.2	22.0
Locus of Control (LOC)				
External chance <sup>a</sup>	26.7 ± 5.2	27.0	27.5 ± 4.6	27.0
Internality	33.8 ± 4.7	33.0	34.3 ± 4.6	34.0
External powerful others <sup>a</sup>	25.9 ± 4.8	26.0	24.8 ± 5.4	25.0
Parenting self-esteem (PSOC)				
Self-efficacy	20.2 ± 4.8	21.0*	19.1 ± 5.1	19.0
Comfort/value of parenting	32.8 ± 5.6	33.0	33.2 ± 5.2	33.0
Overall parental functioning	53.0 ± 6.4	55.0	52.3 ± 6.2	53.0
Personal self-esteem (RSS)-total	31.4 ± 3.9	30.0	31.9 ± 4.0	31.0
Concepts of development (CODQ)				
Categorical <sup>a</sup>	1.4 ± 0.4	1.4	1.4 ± 0.4	1.3
Perspectivistic	1.9 ± 0.2	1.9	2.0 ± 0.3	1.9
Total	1.8 ± 0.2	1.7*	1.8 ± 0.2	1.8
Life stress (LES)				
Positive events	11.6 ± 10.7	9.0*	14.5 ± 11.5	12.0
Negative events <sup>a</sup>	10.2 ± 10.4	7.0	9.8 ± 9.3	7.0
Total events	21.7 ± 7.1	18.0	24.3 ± 16.7	19.0
Balance (positive – negative events)	1.4 ± 12.4	2.0*	4.8 ± 12.6	4.0
Family support (FSS)				
Number of supports	11.5 ± 2.8	11.0*	12.3 ± 2.2	12.0
Value of supports	37.7 ± 12.2	37.0	38.6 ± 10.6	38.0
Family functioning (FACES-III) <sup>b</sup>				
Adaptability	4.3 ± 1.7	4.0	4.0 ± 1.8	4.0
Cohesion	3.5 ± 1.7	3.0	3.5 ± 1.8	3.0
Family type	3.9 ± 1.3	3.5	3.7 ± 1.4	3.5
HOME				
Learning stimulation	6.3 ± 2.8	6.0	5.8 ± 2.6	6.0
Language stimulation	6.3 ± 1.1	7.0	6.3 ± 1.0	7.0
Physical environment	5.3 ± 1.9	6.0	5.6 ± 1.7	6.0
Warmth and acceptance	5.5 ± 1.7	6.0*	5.3 ± 1.5	5.0
Academic stimulation	4.0 ± 1.1	4.0	3.8 ± 1.2	4.0
Modeling	3.0 ± 1.3	3.0	3.2 ± 1.2	3.0
Variety in experience	5.7 ± 1.7	6.0	5.8 ± 1.7	6.0
Acceptance	2.7 ± 1.1	3.0	2.8 ± 1.2	3.0
Total	38.8 ± 8.8	40.0	38.4 ± 8.0	40.0
Number of caregiver changes <sup>a</sup>	0.6 ± 1.0	0**	0.1 ± 0.4	0

<sup>a</sup>Lower scores are better;

<sup>b</sup>central scores are optimal.

\* $p < 0.05$ .

\*\* $p < 0.0001$ .

**Table IV.** Child Assessments at Age 3

	Cocaine-exposed		Nonexposed	
	<i>M</i> ± <i>SD</i>	<i>Mdn</i>	<i>M</i> ± <i>SD</i>	<i>Mdn</i>
Bayley Scales of Infant Development (BSID) <sup>a</sup>				
MDI	83.6 ± 16.7	83.0	84.8 ± 17.9	86.0
PDI	91.8 ± 18.8	96.0	94.9 ± 19.6	100.0
Vineland Adaptive Behavior Scales (VABS) <sup>a</sup>				
Communication	101.0 ± 14.8	105.0	98.8 ± 14.2	99.0
Motor skills	96.6 ± 15.4	96.5	95.5 ± 13.3	93.3

No significant group differences for any of the child assessments at age 3.

<sup>a</sup>Higher scores are better.

circumference (standardized path coefficient = 0.24) and preschool development at age 3 (standardized path coefficient = -0.16). The directionality of the standardized path coefficients indicates that being a male was associated with a larger head circumference and being a female was associated with better preschool development. Caregiver problems demonstrated an indirect influence on preschool development through the quality of the environment. The adjusted birth head circumference directly predicted preschool development (standardized path coefficient = 0.24). Finally, the amount of prenatal cocaine exposure did not significantly predict preschool development. However, it directly affected the adjusted birth head circumference (standardized path coefficient = -0.19) which in turn directly affected preschool development.

## Discussion

The extant literature regarding the psychomotor and cognitive effects of prenatal cocaine exposure on the outcome of children who have been exposed has been inconclusive to date. Although early case reports raised concerns and predicted that there might be significant damage to the central nervous system of children who had been prenatally cocaine exposed, prospective studies have yielded conflicting results and many have documented only subtle differences in outcome.

Recent studies have helped further our understanding of the effects of prenatal cocaine exposure. For example, in the studies by Hurt et al. (2001), findings included group differences in outcome due to environmental factors with no effect of prenatal cocaine exposure, whereas Bennett et al. (2002) found significant gender differences in IQ based on the exposure status of the children.

This study supports the idea that there is no discernable direct effect of cocaine on preschool devel-

opment at age 3. This was demonstrated in the univariate analyses as well as in the SEM. In addition, this study supports the findings from other studies of prenatal cocaine exposure that environmental factors, gender, and head circumference play a role in the long-term outcome.

Most importantly, this study identifies a direct effect of prenatal cocaine exposure on the adjusted birth head circumference, which in turn directly affects preschool development. This has been a robust finding in this cohort, as we have documented this effect in earlier analyses (Behnke et al., 2002) and now again at age 3. This is similar to the findings of Azuma and Chasnoff (1993) that cocaine influenced IQ scores at age 3 through the head circumference at age 3. The crucial difference is that in our sample, we have found an effect of cocaine on the adjusted birth head circumference, not the head circumference at age 3. Also unlike the Chicago sample, by 1 month of age, children in our sample who were cocaine exposed no longer had a significantly smaller mean head circumference than those who were not cocaine exposed. This finding of no drug group difference in head circumference has held true for our cohort from 1 month through age 3 (Sinha, Behnke, Garvan, & Wobie, 1998). It is yet unknown whether this association between adjusted birth head circumference and outcome represents a direct effect of cocaine at the cellular level, decreasing brain growth and thus head circumference, or whether it is merely a marker for the effect of drugs and other risk factors on overall fetal brain development.

This study also begins to tease out the potential effect of environment on the long-term development and how this factor might be associated with prenatal cocaine exposure. The quality of environment was negatively impacted by caregiver problems, and improved preschool development was associated with better quality of the

environment. However, prenatal cocaine use did not directly impact either the caregiver problems or the quality of the environment as we originally hypothesized. It is possible that out-of-home placement plays a role in this finding as over half of the exposed children in our sample no longer live with their biological mother. We speculate that the better scores of the caregivers of the cocaine-exposed children on a few measures may relate to the fact that many of the current guardians are older, perhaps more experienced caregivers. However, our attempts to measure the effect of out-of-home placement by creating a latent variable using the number of caregiver changes during the first 3 years of life did not result in a measurement model with acceptable fit. Thus, this latent variable was dropped from the final model. Further exploration of this important area is ongoing.

Finally, we were interested to discover a relatively large  $R^2$  value for the preschool development outcome. This indicated that the final model accounted for 40% of the variance in developmental outcome at age 3. Although prenatal cocaine exposure contributed to the variance through the adjusted birth head circumference, there was an even greater impact in this model of environment on preschool development.

In summary, in this prospective, longitudinal study of prenatal cocaine exposure, we found no direct effects of prenatal cocaine exposure on preschool development at age 3. In addition, there were no direct effects of prenatal cocaine exposure on caregiver problems or the quality of the environment. However, prenatal cocaine exposure directly affected the adjusted birth head circumference, a result that is consistent with that of earlier studies, and thus through this variable had an indirect effect on preschool development at age 3.

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