SENSORIMOTOR DEVELOPMENT IN COCAINE-EXPOSED INFANTS

Robert Arendt
Lynn Singer
Jennifer Angelopoulos
Case Western Reserve University

Orphia Bass-Busdiecker
JoMarie Mascia
Rainbow Babies and Childrens Hospital

This study investigated effects of prenatal cocaine exposure on infant sensorimotor development. One hundred and sixty-seven 12-month-olds (74 cocaine-exposed and 93 unexposed) were assessed using the Bayley Scales of Infant Development (BSID). Ninety-seven had previously been evaluated on the Movement Assessment of Infants and the Test of Sensory Functions in Infants at age 4 months. On the BSID, the cocaine-exposed infants performed less well on the Mental portion and were more frequently rated as behaviorally suspect. Cocaine-exposed infants also performed less well at four months on the motor and sensory measures. Early motor performance predicted 12 month BSID mental, motor and behavioral outcomes. Cocaine exposure had an effect independent from confounders on general cognitive and specific motor and behavioral outcomes.

sensorimotor development infant prenatal cocaine exposure

INTRODUCTION

Investigators have recently began to study the potential effects of prenatal cocaine exposure on the development of infants (Chasnoff, Burns, Schnoll, & Burns, 1985). This relatively new interest in teratogenic effects of prenatal cocaine exposure occurred in response to the growing use, in the mid-1980s, of a cheap, smokeable form of cocaine, "crack," by women of childbearing age (Lane, 1996). Although evidence indicates that pre-

• **Robert E. Arendt,** Case Western Reserve University, School of Medicine, Department of Pediatrics, 11100 Euclid Ave., Cleveland, OH 44106-6038.

INFANT BEHAVIOR & DEVELOPMENT 21 (4), 1998, pp. 627–640 ISSN 0163-6383

natal cocaine exposure is associated with lower gestational age and growth parameters at birth, even after adjusting for prematurity (Lester, LaGasse, Freier, & Brunner, 1996), the few reports documenting longer term developmental effects have been contradictory (Chasnoff, Griffith, Frier, & Murray, 1992; Chiriboga et al., 1995; Hurt et al., 1995).

A major issue in the developmental consequences of prenatal exposure to a potential toxin is that postnatal environmental factors also play an important role in determining long-term consequences. Sensorimotor skills, as opposed to skills such as language or social interactions, appear to have a greater neurobiological basis, may be relatively less affected by cultural factors, and may be less susceptible to environmental influences (Singer, Yamashita, Lilien, Collin, & Baley, 1997). Thus, early sensorimotor skills may more directly reflect early effects from a potential neurotoxin such as cocaine.

Volpe (1992) presented a convincing summary of potential destructive neural effects secondary to fetal cocaine exposure. Although it was recognized that prenatal development of the central nervous system is susceptible to multiple influences, Volpe argued that in the case of prenatal cocaine exposure, the neurologic system is significantly affected by fetal hypoxemia, caused by impaired placental blood flow, that results in impaired fetal cerebrovascular autoregulation. Such impairments make the fetus highly vulnerable to changes in blood pressure and may lead to hemorrhages in the immediate neonatal period (Singer, Yamashita, Hawkins, Cairns, Baley & Kliegman, 1994). Additionally, constriction of blood vessels after cocaine exposure, documented in animals (Woods, Plessinger, & Clark, 1987), decreases oxygen and nourishment to the fetus, potentially reducing prenatal brain growth.

Several studies have implicated reflexive and motor development as specific components of neurobehavior through which effects of prenatal cocaine exposure might be detected. One measure frequently used to assess early reflexive and motor development in drug exposed populations is the Movement Assessment of Infants (MAI). The MAI systematically evaluates muscle tone, primitive reflexes, automatic reactions, and volitional movements during the first year of life.

Schneider and Chasnoff (1992) tested 30 full-term 4-month-olds prenatally exposed to cocaine and compared their scores on the MAI with scores from 50 unexposed infants selected from a convenience sample. The two groups differed significantly on the total risk score, with the exposed infants acquiring higher risk scores on the muscle tone, primitive reflexes, and volitional movements subscales. Rose-Jacobs, Frank, Brown, Cabral, and Zuckerman (1994) also reported comparisons of cocaine-exposed and unexposed infants at 4 months of age on the MAI. Term infants participating in this study were classified as either heavily cocaine-exposed, lightly cocaine-exposed, or unexposed. Using a regression model, an overall cocaine effect was found for the volitional movements subscale, with more heavily exposed infants having significantly poorer mean scores then either the more lightly exposed or the unexposed.

In a longitudinal study through 15 months, Fetters and Tronick (1996) compared 28 cocaine-exposed infants to 22 unexposed infants who were repeatedly measured on the MAI, the Alberta Infant Motor Scale (Piper & Darrah, 1995), and the Peabody Developmental Motor Scales (Folio & Fewell, 1983). Cocaine exposure had a significant negative effect on motor performance in late infancy. The effect, however, was relatively small when compared to the poor motor performance of both exposed and unexposed groups based on age norms.

Although the evidence is mounting to indicate cocaine produces adverse short-term outcomes, little data are available on long-term consequences. Singer et al. (1997) have reported that children exposed prenatally to cocaine displayed delays in later development when measured on more general measures of

development, such as the Bayley Scales of Infant Development (BSID). Other investigators, however, report no negative effects on the BSID performance attributable to cocaine exposure. Chasnoff reported that cocaine-exposed infants were similar to unexposed infants on the BSID at 24 months of age (Chasnoff et al., 1992) and on the Stanford-Binet Intelligence Scale at 36 months of age (Azuma & Chasnoff, 1993). Hurt et al. (1995) found that, in follow-up through 30 months, BSID Mental and Motor index scores did not differ between a cocaine-exposed and a unexposed group of low socioeconomic status, but that the scores of both groups were substantially lower than published means from children of higher socioeconomic status. Jacobson, Jacobson, Sokol, Martier, and Chiodo (1996) found no effect on BSID Mental or Motor scores based on the presence or absence of cocaine exposure.

In summary, previous findings suggest that cocaine-exposed infants may be at risk of delays in sensorimotor development. Studies of cocaine-exposed infants, however, have often not extended to the long term assessment of outcomes and those longitudinal studies that have been published often have inadequate sample sizes, high attrition rates, contradictory findings, and other methodological problems (Neuspiel, 1995).

The present study reports findings from first year assessments of a longitudinal study of motor development in a group of cocaine-exposed children. Given the potential for cocaine to produce early deficits in sensorimotor development beyond those associated with other risk factors and that those deficits may negatively influence later development, we chose to test the following hypotheses: (a) cocaine-exposed infants will perform less well than a comparable group of unexposed infants at 1 year of age on standardized developmental measures of sensorimotor development, (b) a cohort of cocaine-exposed infants tested at 4 months of age will perform less well on standardized, normative tests of sensory and motor functioning, and (c) a relationship between prenatal cocaine exposure and development will remain after controlling for potential confounders.

METHOD

Participants

This study incorporated a prospective, cohort-sequential design (see Table 1). Infants and young children were recruited simultaneously into two age cohorts of newborns and 1-year-olds. Both cohorts included cocaine-exposed infants and a comparison group of unexposed infants recruited from the same hospital-based population. The study was approved by the Institutional Review Board of the participating hospital and written informed consent was obtained for all participants.

Mothers and infants were recruited from either the newborn nursery at the time of

TABLE 1
Study design: Type of test administered by cohort

	4 Month Visit	*1 Year Visit*
COHORT 1	TSFI & MAI (50/78)	BAYLEY (MDI, PDI & IBR) (41/56)
COHORT 2		BAYLEY (MDI, PDI & IBR) (33/37)

Numbers in parenthesis are number of cocaine-exposed and unexposed infants, respectively.
TSFI = Test of Sensory Functions in Infants;
MAI = Movement Assessment of Infants;
BAYLEY = Bayley Scales of Infant Development

delivery or at a well-baby visit within the first year after delivery. Drug exposure was determined by a combination of medical chart review, maternal and/or infant urine toxicology results, and/or clinical interviews. Urine samples were obtained in the prenatal clinic or at the time of delivery through a hospital screening protocol based on the following risk factors: lack of adequate prenatal care, precipitous delivery, history of drug use, self-reported drug use, previous involvement with the Department of Human Services concerning abuse/neglect of children, intoxication apparent to hospital staff, or impaired cognitive/emotional functioning. Samples were analyzed by enzyme immunoassay using the Syva Emit method (Syva Company, Palo Alto, California), with assays performed for cocaine, barbiturates, amphetamines, marijuana, and heroin. When compared with an anonymous urine screen conducted at the same hospital, 95% of positive women were identified by this combination of clinical indications, chart review, and voluntary urine testing.

Initially, 221 participants were recruited, 91 cocaine-exposed and 130 unexposed. Nine infants, all cocaine negative, were excluded because the mother was less than 17 years old. Two additional pairs (one cocaine-exposed and one unexposed) were excluded because the infant weighed 1500 grams or less at birth. All mothers whose records or interview identified primary psychiatric problems or low intellectual status, those who were positive for HIV, and whose drug tests were positive for PCP, amphetamines, barbiturates or heroin were excluded (n = 10). Women who used alcohol, tobacco, or marijuana during pregnancy were retained in both groups. Thus, 200 infants were scheduled for visits at 4 and/or 12 months (corrected ages) for testing.

Thirty-one of 128 (24%) eligible 4-month-old infants did not return for the 12 month assessment. Of these, 9 (18%) were cocaine-exposed and 22 (28%) were unexposed. Two participants from the 12 month cohort who began the 12 month assessment were unable to complete the testing. Figure 1 includes a breakdown of the cocaine status of the final group of 167.

Measures

Maternal and infant demographic and medical characteristics were collected from medical records. These included maternal age, race, gravidity, number of prenatal visits, and type of medical insurance. Infant birth outcomes included APGAR score, gestational age, length, weight, gender, and head circumference.

The Maternal Post-partum Drug Interview (Streissguth, 1986) was administered to 84 mothers whose infants were recruited at birth to identify and quantify maternal drug use. Mothers were asked to recall the amount and frequency of drug use per day for the month prior to conception and for each trimester of pregnancy. For tobacco use, mothers were asked to recall the number of cigarettes smoked per day, since it was assumed that those who smoked did so every day. Frequency (number of days) of use for alcohol, marijuana, and cocaine use was recorded for the same period. The number of marijuana joints per day and the number of drinks of beer, wine, or hard liquor per day, were also recorded. For cocaine, the number of "rocks" and amount of money spent was also computed. The frequency of use was then multiplied by the amount used per day to compute a severity of use score. Scores from one month prior and the trimesters were then averaged for a mean total severity of use score over the entire pregnancy for each drug. Finally, the scores were subjected to a logarithmic transform to normalize distribution.

The following measures were administered by examiners blinded to drug exposure status:

The Movement Assessment of Infants (MAI) provides a detailed and systematic assessment of motor behavior during the first year of life (Chandler, Andrews, & Swanson, 1980). The 65 item test evaluates muscle tone, primitive reflexes, automatic reactions, and volitional movements from a quantitative and

qualitative perspective. Infants' reflexes, reactions, and movements are rated on a 4 part ordinal scale from most to least mature. Muscle tone is rated on a 6 part scale, ranging from hypotonic through normal to hypertonic. In all areas left/right asymmetries are recorded, while in the muscle tone section upper versus lower extremities distribution variations are also scored. Although normative data are not available, there is an a priori profile for the 4 month age group. A risk point is given for each item scored in the questionable range in each of the four categories and summed for a total risk score. All of the MAI exams were administered by the same licensed physical therapist.

The Test of Sensory Functions in Infants (TSFI) is specifically developed to assess sensory processing and reactivity in 4 to 18 month old infants (DeGangi & Greenspan, 1989). The 24 items evaluate response to tactile deep-pressure, visual-tactile integration, adaptive motor, ocular motor, and reactivity to vestibular stimulation. All TSFI exams were administered by the same occupational therapist, who was certified to administer the test.

The Bayley Scales of Infant Development (BSID) are well-established measures of overall infant cognitive and motor development (Bayley, 1969). The Bayley scales consists of three parts: Mental (PDI), Motor (MDI), and Infant Behavior Record (IBR). The Mental scale is a widely used measure of cognitive development designed to assess, among other abilities, sensory-perceptual activities and discriminations and the ability to respond to the environment. Raw scores on the Mental scale are converted into a standardized Mental Development Index (MDI) score. The Motor scale is designed to provide a measure of gross motor control, coordination abilities, and fine motor manipulatory skills. Performance on the Motor scale produces a standardized Psychomotor Development Index (PDI) score. All of the Bayley exams were administered by the same research assistant, who had been trained by the first author.

The Infant Behavior Record of the BSID assesses the nature of the infant's orientation towards the environment on descriptive rating scales of attitudes, interests, emotions, energy, activity, and tendencies to approach or withdraw from stimulation. Wording and scoring criteria of the individual items varies. We, therefore, chose to use a combination of two methods, employing factors derived from the IBR by Matheny (1980) and IBR risk scores developed by Wolf and Lozoff (1985), to determine whether any group differences could be found on the IBR and whether any statistical differences were clinically relevant.

Matheny (1980) conducted a principal components analysis of the 25 IBR items that are rated on a five- or a nine-point scale and derived five major factors used in the present analyses: Test Affect, Activity, Task Orientation, Audio-Visual Coordination, and Motor Coordination. For the present study, the score a child received on each of these five factors was the sum of raw scores for those items loading on that factor.

Wolf and Lozoff (1985), identified scores on the IBR items that were atypical or deviant from the norm. In addition, they developed a summary variable (General Suspect), a combination of Matheny's (1980) Test Affect and Task Orientation factor scores, to represent a best single indicator of risk. Suspect scores were summed within the five factors developed by Matheny and the General Suspect factor developed by Wolf and Lozoff to investigate clinical relevance of group differences.

Data Analyses

Group Differences

Groups were compared on demographic characteristics using t tests for continuous data and χ^2 analyses for categoric variables. To investigate differences in group means on the BSID, separate analyses of variance were conducted on MDI and PDI scores. Separate mul-

tivariate analysis of variance (MANOVA) of the six IBR factors were done, using those items that make up each factor as dependent variables and cocaine status as the independent variable. MANOVA's of IBR factors were run using raw scores first and then with items coded as suspect or non-suspect.

For those infants who were assessed on the MAI and TSFI, MANOVA's, using the 4 subscales on the MAI or the 5 subscales on the TSFI as dependent variables and drug status as the independent variable, were used to investigate group differences. Pearson product-moment correlations between 4 month measures and 12 month measures were then calculated to explore the relationships between early and later measures.

Confounding Variables and Multivariate Analyses

The following variables were considered as possible confounders: infant race and gender; maternal number of prenatal care visits, marital status, age at delivery, and education; family income and number of persons living in the home. Birth outcomes, including 5 minute APGAR score, gestational age, birth weight, length, and head circumference were also examined as potential confounders and possible mediators. Because of the known prevalence of polydrug use among cocaine users, severity of cigarette, alcohol, and marijuana use was also examined.

For outcomes on which significant group differences were found, a check of relationships between possible confounding variables and outcome variables was conducted, using a correlation at the $p < 0.1$ significance level suggested by Jacobson and Jacobson (1995) as the criterion. Those variables that correlated with the outcomes were then entered into a series of hierarchical multiple regression analyses to assess whether the effects of cocaine remained significant after controlling for all potential confounders. Demographic and prenatal confounding variables were entered first, followed by birth outcomes. Severity of prenatal cigarette, alcohol, and marijuana exposure were entered next, in that order, with cocaine exposure/non-exposure and the summary measure of severity of cocaine use entered alternately on the last step.

RESULTS

Demographic groups differences are shown in Table 2. There were no significant differences in maternal education, ethnicity, or marital status. Cocaine using mothers were significantly older, had higher parity, and received less prenatal care.

All families were receiving public assistance in one or more forms. There were no significant differences in the source of family income between groups. The large majority of both groups were receiving Aid to Dependent Children (ADC) as their primary means of support (89% of the exposed vs. 78% of the unexposed). This subsidy provided the family an income between $5,000 and $10,000 a year, based on family size. Although some of the mothers reported that either they or their partner had work income (9% of the cocaine users and 20% of the non-users), all of the children, both cocaine-exposed and unexposed, qualified for Medicaid assistance. Families receiving Medicaid through this program (Healthy Start) were limited to a reported income of $10,000 to $20,000 a year, depending on the size of the family.

Newborns exposed to cocaine were born at shorter gestation. Infant head circumference and weight at birth were not significantly different after adjusting for gestational age. The cocaine-exposed group had a significantly shorter mean birth length, even after adjustment for gestational age.

There were no differences in head circumference, birth weight, birth length, or 5 minute APGAR between those infants seen only at the four month assessment versus those seen at both four and twelve month assessments. There were no significant differences between those participants who were seen only once

TABLE 2
Sociodemographic characteristics of cocaine-exposed and unexposed groups

	Exposed (n = 74)	*Unexposed (n = 93)*	*t,F or χ^2 test (df)*
Maternal age *M* (SD)	28.0(5.0)	23.0(5.5)	$t(159) = 6.1$***
Parity *M* (SD)	2.7(1.8)	1.6(1.0)	$t(164) = 4.9$***
Prenatal visits *M* (SD)	3.9(4.5)	7.4(3.2)	$t(157) = 5.7$***
Marital Status (%)			$\chi^2(5) = 7.0$
Married	10	13	
Single	76	82	
Divorced	4	1	
Separated	9	2	
Widowed	0	0	
Other (Common Law, Unsure)	1	2	
Maternal Ethnicity (%)			$\chi^2(3) = 4.0$
Black	99	92	
White	1	6	
Hispanic	0	1	
Other(Mixed/Oriental)	0	1	
Maternal Education (%)			$\chi^2(2) = 4.7$
Less than High School	36	30	
High School	45	40	
College	19	30	
Yearly Income (%)			$\chi^2(2) = 4.9$
$0–$10,000	89	78	
$10,000–$20,000	9	20	
Greater than $20,000	2	2	
Work Status (%)			$\chi^2(2) = 5.2$
Full time	7	11	
Part time/at home	11	15	
Unemployed	82	74	
No of People living in Home *M*(SD)	4.3(2.4)	4.2(1.7)	$t(150) = 0.17$
Newborn's Gender (% Female))	47	44	$\chi^2(1) = 0.1$
Infant *M*(SD			
Gest. age (weeks)	37.7(2.2)	38.9(1.8)	$t(159) = 4.0$***
5 Minute APGAR	8.7(1.2)	8.8(0.7)	$t(144) = 0.6$
Head Circ.[a] (cm)	32.9(0.2)	33.4(0.2)	$F(1, 148) = 2.7$
Birth Weight[a] (grams)	2978(58)	3109(50)	$F(1,152) = 2.8$
Birth Length[a] (cm)	47.7(0.3)	48.8(0.2)	$F(1, 148) = 6.6$*

[a] Gestational age covaried;
*$p < .05$ **$p < .01$ ***$p < .001$.

and those who were seen at both times on MAI and TSFI scores.

Severity of Drug Exposure

Mothers who used cocaine (C), when compared to non-users (NC), also smoked more cigarettes per day (C $M = 10.3$ ($SD = 11.2$) and NC $M = 0.9$ ($SD = 2.1$), $t(38) = 5.0$, $p < .001$), consumed more alcoholic drinks per week (C $M = 2.0$ ($SD = 1.7$) and NC $M = 0.2$ ($SD = 0.5$), $t(40) = 6.1$, $p < .001$) and used more marijuana joints per week (C $M = 0.9$ ($SD = 1.6$) and NC $M = 0.0$ ($SD = 0.1$), $t(34) = 3.4$, $p < .001$). These results are consistent with prior reported patterns of polydrug use among pregnant women who use cocaine (Singer et al., 1997).

Developmental Outcomes

Twelve-Months

At 1 year of age, there was a trend for the cocaine-exposed infants to perform less well than the unexposed infants (103.6 vs. 107.6) on the MDI scores, $t(165) = -1.88$, $p = .06$. The mean scores of both groups, however, fell within the normal range. The difference in the groups' PDI scores (101.2 vs. 104.5), while in the same direction, was not significant. Given the difference in the groups' level of prematurity, analyses were repeated adjusting for gestational age. When gestational age was covaried, the cocaine-exposed group also displayed a trend for lower PDI scores (see Table 3).

Results of separate multivariate analysis of variance using IBR raw scores identified significant differences on the Activity, Task Orientation, Visual, Motor, and General factors. After adjusting for gestational age, the Activity, Audio-Visual, and General remained significant, the Task Orientation and Motor factors were reduced to a trend, and the Affect factor became significant (see Table 3).

When the IBR factors were coded as suspect or non-suspect, the cocaine-exposed group exhibited significantly greater suspect behavior on the Activity, Audio-Visual, Test Orientation, and General factors. When gestational age was added as a covariate, the continued difference on the Activity factor, $t(1,148) = 3.2$, $p < .001$, indicated that the infants in the cocaine-exposed group were more often viewed as inactive or listless relative to the unexposed infants. The continued difference on the Audio-Visual factor, $t(1,148) = 2.6$, $p < .01$, after controlling for gestational age indicated a lower interest in sights, sound, and/or tactile exploration among the cocaine-exposed group as compared with the unexposed group. The General factor also remained significant, $t(1,148) = 2.0$, $p < .05$.

Four-Months

In a MANOVA, the cocaine-exposed group performed significantly more poorly on the TSFI and the MAI than the unexposed group, $F(5, 88) = 2.9$, $p < .05$ and $F(4, 90) = 2.8$, $p < .05$, respectively. Both results remained significant after adjusting for gestational age. On the MAI, differences were most evident on the primitive reflexes (3.1 vs. 2.2, $t(93) = 2.0$, $p < .05$) and automatic reactions (1.5 vs. 0.8, $t(93) = 2.6$, $p < .01$) subscales, with the cocaine-exposed group displaying greater risk on both. On the TSFI, the cocaine-exposed group showed significantly poorer performance on the reaction to tactile stimulation (9.1 vs. 9.5, $t(92) = 2.3$, $p < .05$), adaptive (7.2 vs. 8.3, $t(92) = 2.3$, $p < .01$), and visual (7.6 vs. 8.5, $t(92) = 2.8$, $p < .01$) subscales.

Correlations Between 4- and 12-Month Outcome

The 4 month MAI Total Risk score correlated significantly with all three scores from the 12 month Bayley (for MDI $r = -.23$, $p < .05$; for PDI $r = -.36$, $p < .01$; for IBR General Risk Factor $r = .24$, $p < .05$). The TSFI total score did not significantly correlate with any

TABLE 3
Group differences on Bayley scales of infant development

	Exposed (N = 74) M (SD)	*Unexposed (N = 93) M (SD)*	*t or F Test*
Test age (months)	11.9 (0.6)	12.1 (0.5)	$t(1,165) = 2.5$ *
MDI[a]	103.8 (1.6)	107.9 (1.5)	$F(1, 158) = 3.2$ #
PDI[a]	100.6 (1.7)	105.0 (1.5)	$F(1, 158) = 3.5$ #
IBR Factor[a]			
General	3.4 (0.4)	2.3 (0.3)	$F(15, 133) = 2.6$**
Test affect	1.2 (0.2)	0.9 (0.2)	$F(6, 142) = 2.3$*
Activity	0.6 (0.1)	0.2 (0.1)	$F(3, 146) = 3.5$*
Orientation	1.5 (0.2)	1.1 (0.1)	$F(4, 145) = 2.2$#
Audio-Visual	1.5 (0.1)	1.1 (0.1)	$F(3, 145) = 3.6$*
Motor	0.5 (0.1)	0.4 (0.1)	$F(2,147) = 2.7$*

MDI = Mental Development Index;
PDI = Psychomotor Development Index;
IBR = Infant Behavior Record;
[a] Gestational Age Covaried;

**$p < .01$; *$p < .05$; #$p < .10$.

of the Bayley scores. In regression analyses, neither gestational age nor any of the 4 month measures accounted for a significant amount of variance in 12 month scores.

Confounding Variables

The lack of group differences in maternal education, ethnicity, and marital status eliminated those variables from further consideration as confounders. Birth length did not correlate with any of the outcome measures. None of the confounding variables were correlated with the Bayley Mental or Motor Scores. The General Suspect Behavior score, however, correlated with maternal age, $r(148) = .16$, $p = .05$, parity, $r(154) = .13$, $p = .09$, number of prenatal visits, $r(147) = -.14$, $p = .09$, and infant gestational age, $r(148) = -.13$, $p = .10$. On the IBR factors with significant group differences, none of the confounders correlated with Affect or Audio-Visual scores. Maternal age, parity, and number of visits correlated with Activity scores, $r(145) = .24$, $p = .01$, $r(155) = .33$, $p = .001$, $r(148) = -.19$, $p = .02$, respectively.

Maternal age correlated with MAI total score, $r(88) = .18$, $p = .09$. On subscales for which group differences were detected, number of cigarettes and number of drinks per week correlated with Primitive Reflex scores, $r(69) = .29$, $p = .01$ and $r(69) = .20$, $p = .10$, maternal age and number of visits correlated with Automatic Reactions, $r(89) = .20$, $p = .06$ and $r(89) = -.19$, $p = .06$.

Both gestational age and number of prenatal visits correlated with the TSFI total score, $r(92) = -.17$, $p = .09$, and $r(88) = .19$, $p = .07$. On those TSFI subscales that showed group differences, parity, number of prenatal visits, and number of joints per week correlated with Adaptive Motor scores, $r(92) = -.19$, $p = .07$, $r(88) = .24$, $p = .02$, $r(66) = -.24$, $p = .05$; number of prenatal visits and cigarettes per week correlated with Tactile-Visual coordination scores, $r(88) = .20$, $p = .06$, $r(70) = -.27$, $p = .02$; and cigarettes per week correlated with Tactile Reactivity scores, $r(70) = -.21$, $p = .08$.

Effects of Other Factors Versus Cocaine on Outcome

To test the relative influence of confounders, including other drugs, versus cocaine exposure on outcomes, a series of hierarchical regression analyses were performed on those variables in which group differences were identified. In the first series, MAI, TSFI, MDI, PDI, and IBR General Suspect scores were used as the dependent variables. For each outcome, the appropriate confound variables, as described above, were entered on the initial steps. These were followed by severity of cigarette, alcohol, and/or marijuana use where those drugs were identified was a correlate of the outcome considered. On the final step cocaine exposure, coded as exposed or unexposed, and severity of use were alternately entered.

The effect of gestational age was a significant predictor of the total score of the TSFI (see Table 4). Number of prenatal visits also showed a trend towards predicting TSFI total score. After consideration of all potential confounders, cocaine exposure accounted for a trend in TSFI total score. Maternal age displayed a trend towards predicting the total score of the MAI and the IBR General Suspect score.

Result of hierarchical regression on the TSFI subscales indicated that number of prenatal visits predicted Adaptive Motor, while severity of cigarette use displayed a trend in predicting Tactile Responsivity and Visual-Tactile coordination (see Table 5). Cocaine use also showed a trend in predicting Adaptive Motor scores. On the MAI subscales, severity of cigarette use predicted Primitive Reflexes, while maternal age and cocaine exposure, entered last, showed a trend towards predicting Automatic Reactions. On the IBR subscales, maternal age, number of visits, and parity predicted Activity scores.

TABLE 4
Hierarchical regression analyses predicting summary scores

Variable	*B (SE)*	β	ΔR^2
Criterion: TSFI			
Step 1: number of visits	0.21 (0.11)	0.19	0.04#
Step 2: gestational age	−0.54 (0.26)	−0.22	0.04*
Step 3: cocaine use	1.88 (1.02)	0.20	0.04#
Criterion: MAI			
Step 1: maternal age	0.15 (0.09)	0.17	0.03#
Step 2: cigarettes/week	0.99 (0.68)	0.21	0.05
Step 3: cocaine use	−1.75 (1.27)	−0.17	0.00
Criterion: IBR			
Step 1: maternal age	0.08 (0.04)	0.15	0.02#
Step 2: number of visits	−0.08 (0.06)	−0.11	0.01
Step 3: parity	0.28 (0.17)	0.14	0.01
Step 4: gestational age	−0.13 (0.13)	−.08	0.00
Step 5: cocaine use	−0.67 (0.54)	−0.11	0.01

MAI = Movement Assessment of Infants Total Risk Score
TSFI = Test of Sensory Functions in Infants Total Score
IBR = Infant Behavior Record General Suspect Score
#$p < .10$; *$p < .05$.

TABLE 5
Hierarchical regression analyses predicting subscale scores

Variable	*B (SE)*	β	ΔR^2
TSFI			
Criterion: Tactile Responsivity			
Step 1: cigarettes/week	−0.13 (0.07)	−0.20	0.04#
Step 2: cocaine use	0.30 (0.27)	0.20	0.02
Criterion: Adaptive Motor			
Step 1: number of visits	0.12 (0.05)	0.24	0.06*
Step 2: parity	−0.20 (0.14)	−0.15	0.02
Step 3: marijuana joints/week	−1.02 (0.76)	−0.17	0.05
Step 4: cocaine use	0.81 (0.46)	0.19	0.03#
Criterion: Visual-Tactile			
Step 1: number of visits	0.07 (0.04)	0.20	0.04#
Step 2: cigarettes/week	−0.27 (0.16)	−0.20	0.06#
Step 3: cocaine use	0.72 (0.61)	0.22	0.02
MAI			
Criterion: Primitive Reflexes			
Step 1: cigarettes/week	0.57 (0.22)	0.29	0.08*
Step 2: drinks/week	−0.08 (0.50)	−0.02	0.04
Step 3: cocaine use	−0.61 (0.83)	−0.13	0.01
Criterion: Automatic Reactions			
Step 1: maternal age	0.04 (0.02)	0.19	0.04*
Step 2: number of visits	−0.05 (0.03)	−0.17	0.03
Step 3: cocaine use	−0.55 (0.30)	−0.22	0.03#
IBR			
Criterion: Activity			
Step 1: maternal age	0.03 (0.01)	0.23	0.05**
Step 2: number of visits	−0.03 (0.01)	−0.18	0.03*
Step 3: parity	0.14 (0.04)	0.28	0.07**
Step 4: cocaine use	−0.05 (0.14)	−0.04	0.00

MAI = Movement Assessment of Infants Total Risk Score;
TSFI = Test of Sensory Functions in Infants Total Score;
IBR = Infant Behavior Record General Suspect Score;
#$p < .10$; *$p < .05$; **$p < .01$.

DISCUSSION

The current study found that infants exposed to cocaine during gestation were also more likely to be exposed to other known teratogens, particularly, alcohol, nicotine and marijuana. At 4 months of age, these drug exposed infants displayed poorer sensory reactivity and an at-risk level of motor development in comparison to a group of infants of similar race, gender, age, and socioeconomic status whose mothers did not use cocaine during pregnancy.

At 12 months, the drug exposed group showed a trend to perform less well than the unexposed group on the mental portion of the Bayley Scales of Infant Development. Drug exposed 1-year-olds were also more likely to exhibit behavior rated atypical and less adaptive than the comparison group. Because scores from the Bayley Mental Scale and the Affect and Audio-Visual subscales of the Bayley IBR were not correlated with any of the confounding variable, group differences on these outcomes may be independent effects of cocaine exposure. The early motor measure (MAI), but not the early sensory measure (TSFI) was significantly correlated with 12 month outcome on the Bayley Scales.

After accounting for confounders, cocaine exposure also accounted for a trend in the variance of the TSFI total score, Adaptive Motor subscale of the TSFI, and the Automatic Reactions subscale of the MAI. Maternal age accounted for a tend in the variance of the MAI total score and the IBR General score and, in addition to cocaine exposure, parity accounted for a significant proportion of variance in the IBR Activity factor. The number of cigarettes smoked per week by mothers was a significant predictor of the MAI Primitive Reflex subscale score, and a trend on the Tactile Responsivity and Visual-Tactile subscales of the TSFI. Because number of cigarettes represents severity of exposure, these finding suggest a dose response.

Differences on the Primitive Reflexes and Automatic Reactions subscales of the MAI suggest a disruption in the typical course of neurological maturation. Similarly, TSFI subscale differences suggest specific sensory disruptions in children prenatally exposed to drugs.

Differences found on the IBR suggest that the scale detected clinically relevant differences in the behavior of 12-month-olds related to both prenatal factors such as maternal age, number of prenatal visits and parity, as well as 4-month-old motor performance. Although scores from the Mental and Motor portions of the BSID are not considered predictive of later development, Wolf and Lozoff (1985) found relative consistency in the distributions of ratings between 6 and 30 months of age.

Findings from the IBR factors also prompt the notion that differences reported in the performance of drug-exposed children may be related to low level of energy and movement (Activity), a relative lack of attention to sights and sounds (Audio-Visual), and difficulty in interactions with caregivers (Affect) related to at-risk prenatal factors. These results, however, are also consistent with the model proposed by Lester and Tronick (1994) of negative prenatal drug exposure effects on an infant's neuroregulatory capacity to control attention, arousal, affect, and action. Further follow-up of the infants will be necessary to determine if reliable differences in activity, attention, and affect associated with prenatal drug exposure can be identified at older ages.

There are several limitations to the present study. Although presence or absence of cocaine exposure was established through a review of medical records that included urine drug testing and interviews, quantification of cocaine use and other drug use was based on maternal report, which may be unreliable (Zuckerman, Amaro, & Cabral, 1989). We had made extensive efforts to establish a rapport with the mothers and to assure them the information was confidential to minimize incentives to misrepresent use. In a study conducted on a different sample of infants born to women recruited from the same inner-city population, only 9 mothers of 143 identified cocaine users denied use and were subsequently identified through meconium analyses (Arendt, Singer, Minnes, Robinson, & Salvator, 1998). In other words, 94% of cocaine using women were identified by a similar combination of clinical indications, historical information, and voluntary urine testing used in the current study.

Another question arises, however, because of the retrospective nature of the drug data. Given the time between the actual drug use and the interview, it is likely that, even with a sincere effort, the mothers were able to provide only rough estimates of their drug use.

Had we been able to collect more reliable information, either through prenatal interviews, meconium or hair analysis, we would have had greater power to detect differences between infant outcomes.

Although assessments were done by examiners masked to drug exposure status, infants were tested with their caregivers present and it may have been possible to identify exposure status from infant or caregiver's characteristics or behaviors. The possibility of examiner bias, therefore, cannot be ruled out.

Although the findings of early negative effects in motor development of drug exposed infants in this study support a neurological mechanism, it is important to note that the influence of environmental factors cannot be overlooked. This is particularly evident from the small amount of variance in the 12 month outcome scores accounted for by prenatal drug exposure. Other postnatal factors, such as parenting practices, life style, or maternal mental health, are likely to have varied between groups because of drug use (Singer et al., 1995) and these factors have a major role to play in a child's development (Singer, Arendt et al., 1997).

Acknowledgments: Supported by grants from the National Institute on Drug Abuse R29-07358 and R01-07957. Thanks to the mothers and staff at the Center for the Advancement of Mothers and Children; also the Cleveland Foundation, the Sihler Mental Health Foundation, the Woodruff Foundation, and the Rainbow Board of Trustees, which funded clinical services. Portions of this article were presented at the Society for Pediatric Research Annual Meetings, Seattle WA, 1994 and San Diego CA, 1995.

REFERENCES

Arendt, R., Singer, L., Minnes, S., Robinson, J., & Salvator, A. (1998, April). *Accuracy in detecting prenatal drug exposure.* Paper presented at the XIth International Conference on Infant Studies, Atlanta, GA.

Azuma, S., & Chasnoff, I. (1993). Outcome of children prenatally exposed to cocaine and other drugs: A path analysis of 3 year data. *Pediatrics, 92,* 396–402.

Bayley, N. (1969). *Bayley scales of infant development.* New York: Psychological Corp.

Chandler, L. S., Andrews, M. S., & Swanson, M. W. (1980). *Movement of infant assessment: A manual.* Rolling Bay, WA: Authors.

Chasnoff, I. J., Burns, W. J., Schnoll, S. H., & Burns, K. A. (1985). Cocaine use in pregnancy. *New England Journal of Medicine, 313,* 666–669.

Chasnoff, I. J., Griffith, D. R., Freier, C., & Murray, J. (1992). Cocaine/polydrug use in pregnancy: Two year follow-up. *Pediatrics, 89,* 284–289.

Chiriboga, C. A., Vibbert, M., Malouf, R., Suarez, M. S., Abrams, E. J., Heagarty, M. C., Brust, J. C. M., & Hauser W. A. (1995). Neurological correlates of fetal cocaine exposure: Transient hypertonia of infancy and early childhood. *Pediatrics, 96,* 1070–1077.

DeGangi, G. A., & Greenspan, S. I. (1989). *Test of sensory functions in infants.* Los Angles: Western Psychological.

Fetters, L., & Tronick, E. Z. (1996). Neuromotor development of cocaine exposed and control infants from birth through 15 months: Poor and poorer performance. *Pediatrics, 98,* 938–943.

Folio, M. R., & Fewell, R. R. (1983). *Peabody developmental motor scales and activity cards manual.* Allen, TX: DLM Teaching Resources.

Hurt, H., Brodsky, N. L., Betancourt, L., Braitman, L. E., Malmud, E., & Giannetta, J. (1995). Cocaine exposed children: Follow-up through 30 months. *Developmental and Behavioral Pediatrics, 16,* 29–35.

Jacobson, J. L., & Jacobson, S. W. (1995). Strategies for detecting the effects of prenatal drug exposure: Lessons from research on alcohol. In M. Lewis, & M. Bendersky (Eds.), *Mothers, babies, and cocaine* (pp. 111–127). Hillsdale, NJ: Erlbaum.

Jacobson, S. W., Jacobson, J. L., Sokol, R. J., Martier, S. S., & Chiodo, L. M. (1996). New evidence for neurobehavioral effects of in utero cocaine exposure. *Journal of Pediatrics, 129,* 581–590.

Lane, S. J. (1996). Cocaine: An overview of use, actions, and effects. In L.S. Chandler, & S. J. Lane (Eds.), *Children with prenatal drug exposure* (pp. 15–33). New York: Haworth.

Lester, B. M., LaGasse, L., Frier, K., & Brunner, S. (1996). Studies of cocaine-exposed infants. In C. L. Wetherington, V. L. Smeriglio, & L. P. Finnegan (Eds.), *Behavioral studies of drug-exposed offspring: Methodological issues in human and animal research.* (NIDA Research Monograph 164, NIH Publication No. 96-4105, pp. 175–210). Rockville, MD: National Institutes of Health.

Lester, B. M. & Tronick, E. Z. (1994). The effects of prenatal cocaine exposure and child outcome: Lessons from the past. *Infant Mental Health Journal, 15,* 107–120.

Matheny, A. P., Jr. (1980). Bayley's Infant Behavior Record: Behavioral components and twin analyses. *Child Development, 51,* 1157–1167.

Neuspiel, D. R. (1995). The problem of confounding in research on prenatal cocaine effects on behavior and development. In M. Lewis, & M. Bendersky (Eds.), *Mothers, babies, and cocaine* (pp. 95–109). Hillsdale, NJ: Erlbaum.

Piper, M. C., & Darrah, J. (1995). *Alberta infant motor scale.* Philadelphia, PA: W.B. Saunders.

Rose-Jacobs, R., Frank, D. A., Brown, E. R., Cabral, H., & Zuckerman, B. S. (1994). Use of the movement assessment of infants (MAI) with in-utero cocaine exposed infants. *Pediatric Research, 35,* part 2, 26A.

Schneider, J. W., & Chasnoff, I. J. (1992). Motor assessment of cocaine/polydrug exposed infants at 4 months. *Neurotoxicology and Teratology, 14,* 91–101.

Singer, L., Arendt, R., Farkas, K., Minnes, S., Huang, J., & Yamashita, T. (1997). The relationship of prenatal cocaine exposure and maternal postpartum psychological distress to child developmental outcome. *Development and Psychopathology, 9,* 473–489.

Singer, L., Arendt, R., Minnes, S., Farkas, K., Yamashita, T., & Kliegman, R. (1995). Increased psychological distress in post-partum, cocaine-using mothers. *Journal of Substance Abuse, 7,* 165–174.

Singer, L., Yamashita, T., Hawkins, S., Cairns, D., Baley, J., & Kliegman, R. (1994). Increased incidence of intraventricular hemorrhage and developmental delay in cocaine exposed, very low birth weight infants. *The Journal of Pediatrics, 124,* 765–771.

Singer, L. T., Yamashita, T. S., Lilien, L., Collin, M., & Baley, J. (1997). A longitudinal study of infants with bronchopulmonary dysplasia and very low birth weight. *Pediatrics, 100,* 987–993.

Streissguth, A. P. (1986). The behavioral teratology of alcohol: Performance, behavioral, and intellectual deficits in prenatally exposed children. In J. R. West (Ed.), *Alcohol and brain development* (pp. 3–44). New York: Oxford University Press.

Volpe, J. J. (1992). Effect of cocaine use on the fetus. *New England Journal of Medicine, 327,* 399–407.

Wolf, A. W., & Lozoff, B. (1985). A clinically interpretable method for analyzing the Bayley Infant Behavior Record. *Journal of Pediatric Psychology, 10,* 199–214.

Woods, J. R., Plessinger, M. A., & Clark, K. E. (1987). Effect of cocaine on uterine blood flow and fetal oxygenation. *Journal of the American Medical Association, 257,* 957–961.

Zuckerman, B., Amaro, H., & Cabral H. (1989). Validity of self-reporting of marijuana and cocaine use among adolescents. *Journal of Pediatrics, 115,* 812–815.

24 February 1997; Revised 25 March 1998 ■