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Relationship of prenatal cocaine exposure and maternal postpartum psychological distress to child developmental outcome

LYNN SINGER[a], **ROBERT ARENDT**[a], **KATHLEEN FARKAS**[b], **SONIA MINNES**[a], **JIE HUANG**[a], and **TOYOKO YAMASHITA**[a]

[a]Department of Pediatrics, Case Western Reserve University School of Medicine

[b]The Mandel School of Applied Social Sciences, Case Western Reserve University

Abstract

Maternal cocaine use during pregnancy can affect the infant directly through toxic effects or indirectly through cocaine's influence on maternal psychological status. We followed 160 cocaine exposed and 56 nonexposed infants and their mothers identified at birth through interview and/or urine screen. Although cocaine exposure defined the groups, infant exposure to alcohol, marijuana, and tobacco was allowed to vary. Infants were 99% African American and poor. All mothers completed the Brief Symptom Inventory (BSI) and infants were given the Bayley Scales of Mental (MDI) and Motor (PDI) Development at a mean corrected age of 17 ± 8 months. Both MDIs (94 ± 17 vs. 103 ± 16) and PDIs (101 ± 16 vs. 108 ± 12) were lower for cocaine exposed infants. Psychological distress was greater in cocaine using mothers. Hierarchical multiple regression was used to assess the relative effects of gestational age, maternal psychological distress, and cocaine and polydrug exposure on infant outcomes. Both psychological distress and cocaine and alcohol exposure predicted lower MDIs after controlling for prematurity. Neither psychological distress nor alcohol exposure predicted motor outcome, while cocaine had a significant effect. Tobacco and marijuana exposure were unrelated to outcome. These findings provide further support for direct effects of cocaine and alcohol on infant development, as well as highlight the need for studies to document maternal psychological factors, which may increase child risk for poorer outcomes.

Introduction

Because, over the past decade, prenatal cocaine exposure has affected and continues to affect 5–15% of infants born in urban areas of the United States, concerns have been raised about the potential for long-term, negative developmental sequelae (Neuspiel, Hamel, Hochberg, Greene, & Campbell, 1991; Singer, Garber, & Kliegman, 1991). A growing body of well controlled studies have used animal models to document neurotoxic properties of

Address correspondence and reprint requests to: Lynn Singer, Ph.D., The Triangle Building, Department of Pediatrics, Case Western Reserve University School of Medicine, 11400 Euclid Avenue, Suite 250-A, Cleveland, OH 44106.

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cocaine capable of producing negative developmental effects in exposed fetuses (Spear, 1996; Thadani, 1995). Although the generalizability of animal research to human outcomes is not clear cut (Morishima & Whittington, 1995; Needlman, Frank, Augustyn, & Zuckerman, 1995), studies with human neonates also suggest that in utero exposure to cocaine is associated with atypical neurobehavioral outcomes in newborns (see Singer, Arendt, & Minnes, 1993 or Volpe, 1992, for reviews).

Plausible mechanisms for cocaine's direct and indirect negative effects on central nervous system development have been proposed (Neuspiel et al., 1991; Volpe, 1992). These pathways include direct structural damage to the developing fetal brain through aminergic mechanisms and fetal hypoxemia due to catecholamine mediated placental vascular compromise (Kosofsky, 1991; Webster, Brown–Woodman, Lipson, & Ritchie, 1991). Because of the high prevalence of drug use in poor urban populations, poverty, increased child neglect and abuse, and an impaired social environment with dysfunctional caregiving have also been considered as contributors to negative sequelae for drug exposed children (Hans, Bernstein, & Hensen, 1990; Lief, 1985; Mayes, Granger, Bornstein, & Zuckerman, 1992; Rosen & Johnson, 1982; Singer, Arendt, & Minnes, 1993).

Studies of developmental outcome beyond the neonatal period, however, remain sparse and contradictory. For example, Mayes, Bornstein, Chawarska, and Granger (1995) assessed developmental outcomes via the Bayley Scales in 108 3-month-olds, 61 of whom had been prenatally exposed to cocaine. Compared to the non-drug exposed group, the cocaine exposed group demonstrated relatively poorer performance on the Motor scale but not on the Mental scale. In contrast, a relatively small study of light, "social" cocaine users found that their offspring were not different at assessment on the Bayley Scales at 20 months of age from infants born to a nonuse comparison group (Graham, 1992).

Chasnoff and colleagues (Azuma & Chasnoff, 1993; Chasnoff, Griffith, Freier, & Murphy, 1992; Griffith, Azuma, & Chasnoff, 1994) have followed a prospectively recruited cohort of cocaine exposed infants to 3 years. As in other studies, cocaine exposed children were exposed to a number of other drugs in addition to cocaine. At 2 years, no differences based on drug exposure were found. By 3 years, deficits in verbal reasoning on Stanford–Binet outcomes, as well as attentional problems and more aggressive behavior in cocaine exposed children were detectable. The negative outcomes were more striking in light of early identification of maternal cocaine use and intensive treatment efforts during maternal pregnancy and after childbirth. Overall IQ scores, however, were not statistically different from controls. Similarly, in a large, prospective, blinded follow-up of cocaine exposed infants to 30 months, Hurt and colleagues (Hurt, Brodsky, Betancourt, Braitman, Malmud, & Gianetta, 1995) repeatedly administered the Bayley Scales at 6, 12, 18, and 24 months of age. They found no differences between groups at any age tested.

Because of the putative role of social/environmental factors on child outcomes (Sameroff & Chandler, 1975), several specific aspects of the caregiving environment affected by maternal drug use have also been explored. The quality of home environment was found to mediate the negative effects of cocaine and polydrug exposure on 3-year IQ in one study (Azuma & Chasnoff, 1993). In another report, out of home placement was found to be more frequent in

a cohort of very low birthweight infants who were cocaine exposed, compared to a matched, nonexposed comparison group. Placement, however, was unrelated to the more delayed development of the exposed group (Singer, Yamashita, Hawkins, Cairns, Baley, & Kliegman, 1994).

In other studies of attachment behavior of cocaine and PCP exposed infants, drug exposed infants were found to be disorganized and insecurely attached to their caregivers, suggesting that emotional disturbances in cocaine exposed cohorts may compromise child developmental outcomes (Rodning, Beckwith, & Howard, 1991). In studies of methadone maintained mothers, maternal psychopathology and decreased psychological resources were related to poorer maternal child interactions at 4 and 24 months of age (Hans, Bernstein, & Hensen, 1990).

Specific to cocaine users, extended use frequently results in psychological distress symptoms that replace the initially attractive feelings of euphoria produced by the drug. Poor motivation, personality disorders, and impaired social interactions of users, all of which may affect infant caregiving, have been reported (Griffin, Weiss, Mirin, & Lange, 1989; Kleinman et al., 1990; Newcomb, Bentler, & Fahy, 1987). Recent studies of poor, urban, cocaine using mothers postpartum found higher self-reports of psychological distress symptoms, especially interpersonal difficulties, paranoid ideation, and phobic anxiety, causing concerns that such symptoms may interfere with maternal provision of a responsive caregiving environment for her infant (Singer, Farkas, Arendt, Minnes, Yamashita, & Kliegman, 1995).

Maternal psychological distress, especially depression, has been identified as a major risk factor in child development, as infants may be negatively affected by the unresponsive or rejecting interactions of depressed caregivers (Cohn & Tronick, 1983; Field, Sandberg, Garcia, Vega–Lahr, Goldstein, & Guy, 1985). Mother–child interactions are particularly relevant to the development of child cognitive, language, attentional, and behavioral capacities, and a number of studies have documented poorer functioning in these areas in children of depressed mothers (Cogill, Caplan, Alexandra, Mordecai–Robson, & Kumar, 1986; Radke–Yarrow, Cummings, Kochanska, & Chapman, 1984; Wrate, Rooney, Thomas, & Cox, 1985).

The relationships among infant biological risk due to cocaine and other drug exposure, maternal psychological distress, and child developmental outcomes are particularly complex and are also dependent on a host of other factors, including the number of other life stressors, socioeconomic status, and the availability of social supports (Weinraub & Wolf, 1983). The present study used a transactional model of development, in which infant biologic risk was hypothesized to interact with maternal psychological distress to affect child outcomes over time (Sameroff & Chandler, 1975). Maternal distress was evaluated as a factor potentially mediating the effects of cocaine and other drug exposure on outcomes (i.e., because cocaine using women have more symptoms of psychological distress which could alter mother–child interactions and eventual outcome, poorer child outcomes could be a function of these impairments rather than due to direct biologic effects). Alternatively, maternal distress postpartum could pose additional and independent risk to the biologic

effects of fetal drug exposure, or maternal distress could be a moderator of the effects of cocaine exposure, i.e., cocaine exposed or nonexposed infants could be differentially affected by maternal psychological distress (Baron & Kenny, 1986).

The present study investigated developmental outcomes of cocaine exposed and non-exposed infants of poor, African American women whose children were followed in a specialized, pediatric well-child care clinic until 2 years of age. Cocaine exposure was hypothesized to relate to poorer developmental outcomes. All mothers were also assessed postpartum regarding their experience of psychological distress symptoms. The effects of cocaine exposure on developmental outcome were examined relative to the effects of the severity of maternal psychological distress, as well as relative to the impact of other drugs, because of the known prevalence of polydrug use in cocaine using populations (Richardson & Day, 1994; Singer, Arendt, Song, Warshawsky, & Kliegman, 1994; Zuckerman et al., 1989). In particular, cocaine exposed infants have been shown to have greater exposure to alcohol, marijuana, and tobacco during fetal development, all of which have been associated with less optimal developmental outcomes in prior studies (Brown et al., 1991; Fried & Watkinson, 1990; Jacobson, Jacobson, Sokol, Martier, & Ager, 1993; Streissguth, 1986a, 1986b).

Method

Subjects

Two hundred and sixteen postpartum women (160 cocaine using, 56 cocaine nonusing) and their infants were recruited from a high risk infant follow-up program at a large, urban teaching hospital. Ninety-nine percent of women and their infants were African American, and all were receiving public assistance. Cocaine positive and negative groups were determined by maternal or infant urine drug screen and clinical interview at the time of delivery. Urine samples were obtained immediately before or after labor and delivery and were analyzed for the presence of cocaine's primary metabolite, benzoylecgonine, and for barbiturates, marijuana, and opiates. The Syva Emit method (Syva Company, Palo Alto, CA) was used for the analysis. The specificity for benzoylecgonine was 99% at a concentration of 0.3 mg/mL. Follow-up gas chromatography analyses were not performed.

The hospital performs urine toxicology screens for drugs on all women who receive no prenatal care, appear to be intoxicated or taking drugs, who have history of involvement with the Department of Human Services in previous pregnancies, or who self-admit or appear to be high risk for drug use after interview by a clinical social worker. From this pool of high risk women, both positive and negative groups were formed, and all mothers were invited by a pediatric nurse practitioner to participate in a specialized well-child care clinic, with enhanced social services and cab/bus vouchers provided for transportation.

The control group was comprised of women with the same race, social class, and high risk status but who were negative for cocaine use based on both urine screen and clinical interview results. Use of both urine screen and clinical history allowed maximum identification of cocaine using women and minimized the number of women who might be misidentified. Women who used alcohol, marijuana, or tobacco during pregnancy were

included in both groups. Women who were excluded from both groups included those referred to the clinic because of psychiatric problems or low intellectual status, those who were positive for HIV, or whose drug tests were positive for PCP, amphetamines, barbiturates, and heroin. Infants who were very low birthweight (i.e., <1500 g), who had other significant medical risk conditions, or who were placed in the neonatal intensive care unit at birth were also excluded.

Procedures

Infants were scheduled for developmental follow-up at 6, 12, 18, and 24 months of age (corrected for prematurity) as part of their pediatric care. Assessment of maternal psychological distress and an extensive interview concerning cocaine, alcohol, marijuana, and cigarette use during pregnancy were administered to each mother as soon as possible after the birth of her child. Specific measures included the following:

The Bayley Scales of Infant Development (Bayley, 1969, 1993) are widely used assessments of infant mental and psychomotor development. The mental development index (MDI) is a standard score reflecting sensory perceptual acuities, discrimination skills and the acquisition of object constancy, memory, learning, and problem solving abilities. The psychomotor index (PDI) is a measure of gross motor control, coordination abilities, and fine motor manipulation. For the present investigation, the MDIs and PDIs used in final analyses were those from the oldest age at which a child was tested in order to maximize sample size, and to enhance generalizability, as well as the predictive validity, of the assessment.

The Brief Symptom Inventory (BSI; Derogatis, 1992) is a standardized 53 item, self-report questionnaire designed to evaluate a range of psychiatric symptoms. For the present study, a global index of symptom severity, the General Severity Index (GSI), was used. Cronbach's α for global and individual scales ranged from .71 to .83. Test–retest reliability varies from .68 to .91. Validity has been demonstrated through its relationship to content scales and cluster scores of the Minnesota Multiphasic Personality Inventory (MMPI), with r values varying from .30 to .72.

The Peabody Picture Vocabulary Test (PPVT; Dunn & Dunn, 1981) is a brief screening measure used to assess maternal verbal comprehension. Internal consistency ranges from .73 to .84 and test–retest reliabilities vary from .76 to .79. The PPVT-R is highly correlated with various IQ scales, as well as maternal education (Jacobson, Jacobson, & Frye, 1991; Needlman, Singer, Lewis, & Yamashita, 1996).

The Maternal Post-Partum Questionnaire (Streissguth, 1986a, 1986b) was used to quantify maternal drug use the month prior to and during each trimester of pregnancy and to document drug taking behavior, such as age of first use. For the month prior to pregnancy, and for each trimester of pregnancy, mothers were requested to recall frequency and amount of drug use. For tobacco, the number of cigarettes smoked per day was recorded. For marijuana, the number of joints per day, and for alcohol, the number of absolute ounces of beer, wine, or hard liquor per day was computed. For cocaine, the number of rocks and

amount of money spent per day were noted. For each drug, the frequency of use was recorded on a Likert type scale ranging from 0 (not at all) to 7 (daily use). The frequency of use was multiplied by the amount used per day to compute a severity of use score for the month prior to pregnancy and for each trimester. This score was then averaged for a total score for the prenatal exposure for each drug.

Demographic and medical characteristics at the time of infant birth were taken from hospital birth record. These included maternal race, age, gravida, number of prenatal care visits, and type of medical insurance. Information on foster care placement was also noted at follow-up. This study was approved by the Institutional Review Board of the participating hospital, and maternal written informed consent was obtained for infant participation.

Data analyses

Groups were compared on demographic characteristics, maternal distress scores, vocabulary, birth, and developmental outcome measures using *t* tests for continuous data and χ^2 analyses for categoric variables. Analyses of covariance were used to compare developmental outcomes with control for infant prematurity or age at testing and to compare duration of maternal drug usage between groups, with control for maternal age. Pearson product moment correlations were calculated to assess the relationships of maternal substance use, psychological distress, and vocabulary to child outcomes.

A series of hierarchical multiple regression equations were also calculated to assess the relative contributions of prenatal cocaine exposure, maternal psychological distress, prematurity, and cigarette, alcohol, or marijuana exposure to infant mental and motor outcomes. First, two separate hierarchical regression analyses were run for each of the neurobehavioral outcomes (MDI and PDI) in order to assess the effects of cocaine exposure on outcomes, after controlling for the effects of other drugs. For these analyses, prematurity (GA) was not controlled, because it is known to be affected by alcohol and cocaine exposure. Controlling for prematurity is likely to contribute to Type II error since none of the variance shared by gestational age and alcohol or cocaine would be attributed to these drugs in the analyses (see Jacobson, Jacobson, Sokol, Martier, & Ager, 1993; Streissguth, Barr, Sampson, Parrish–Johnson, Kirchner, & Martin, 1986). For each outcome, maternal vocabulary and control drugs of cigarette, alcohol, and marijuana were evaluated first, in that order, if they were potential confounders. Drugs were considered as possible confounders if they were even weakly ($p < .10$) related to outcome. Order of entry was determined based on prevalence of use and legality of drug, with the most prevalent and legally used drugs entered first. Cocaine exposure was entered on the last step.

To evaluate maternal psychological distress as a mediator of cocaine's effects on outcomes, a second set of hierarchical regressions was computed. Maternal distress was examined separately because its relationship to maternal drug use is unclear. It can be both a consequence and a cause of drug use. In these analyses, prematurity was controlled because maternal psychological distress has been found to be related to infant prematurity (Blumberg, 1985; Brooten et al., 1988; Singer, Bruening, Davillier, Hawkins, & Yamashita, 1996).

The mediating role of maternal distress was evaluated using the criteria outlined by Baron & Kenny (1986) (i.e., independent variables should be significantly associated with the dependent variable, the mediating variable should show significant relations to both the independent and dependent variables, and statistical control of the mediating variable should substantially reduce relations between the independent and dependent variables). Thus, if maternal distress were the mediating variable linking child mental or motor outcomes (the dependent variables) to cocaine exposure (the independent variable) after control for prematurity, then maternal distress should be related significantly to child outcomes and to cocaine exposure and removal of the effects of maternal psychological distress should significantly lessen (partial mediation) or remove (mediation) the relationship of exposure to outcome. Maternal distress symptoms were also evaluated as a moderator of cocaine's effects on outcome. For this evaluation, an interaction term (cocaine exposure × maternal distress [GSI]) was entered into the regression equation after evaluation of the direct effects of cocaine, maternal distress, and confounding variables on outcome.

Results

Group characteristics

Demographic and medical characteristics of the two groups are presented in Table 1. As in other reports (Hadeed & Siegal, 1989; Singer, Arendt, Song, Warshawsky, & Kliegman, 1994), cocaine using women were older and had more previous pregnancies. There was a trend ($p < .10$) for cocaine using women to be less likely to have received prenatal care. Their infants were of lower gestational ages, even though very low birthweight infants or infants in neonatal intensive care had been excluded from this sample. Once gestational age was controlled, growth parameters at birth did not differ.

Cocaine using women did not differ from controls on vocabulary score, although the mean for both groups was more than one standard deviation below the average reported for the normative group for the scale. As noted in Table 2, cocaine using women were more likely to have used alcohol, marijuana, and tobacco for longer periods of time, even after adjustment for maternal age differences. Tables 2, 3, 4, and 5 give results of the clinical questionnaire documenting history of drug use during pregnancy. For all drugs and trimesters, cocaine using women used alcohol, tobacco, and marijuana more frequently and in higher amounts than cocaine nonusers. For cocaine nonusers, lowest frequency and amounts for all drugs, except marijuana, were reported in the third trimester. In particular, frequency of alcohol use was reported to be reduced by half from the month prior to pregnancy to the third trimester, and the amount consumed per day was reduced by two-thirds.

Developmental Outcome

From the original identified group, at least one follow-up visit for a Bayley evaluation was completed for 151 infants, representing 70% of the original group. A series of *t* tests comparing demographic and birth characteristics of those infants who returned versus those who did not return for follow-up indicated there was no differences in occurrence of pre-natal care, maternal gravida, age, use of tobacco and marijuana during pregnancy, or

maternal psychological distress. Infants were not different in gender or on any birth parameter. The only difference between groups was that mothers who did not return were less likely to have used alcohol during pregnancy ($t[df\ 1, 195] = 1.9$, $p < .06$).

Comparisons of developmental outcomes of infants at follow-up are noted in Table 6. Infants did not differ in chronologic or corrected ages. Both Bayley MDI and PDI scores were significantly lower for the cocaine exposed group, after controlling for prematurity. Mean scores for both exposed and nonexposed infants, however, were within the average range. Because the Bayley scores used were from the oldest age of testing the child, analyses were rerun using age of Bayley testing as a covariate. There were no effects on PDI, ($F[1, 146] = .24$, $p < .62$). There were significant effects of age at testing on MDI, ($F[1, 152] = 14.5$, $p < .001$), but they did not influence group differences, which remained significant ($F[1, 152] = 8.8$, $p < .005$). Follow-up analyses indicated that older age at testing was associated with a lower MDI score consistent with other studies which have used the Bayley Scales (Hurt et al., 1995).

Fourteen of the cocaine exposed children had been placed in foster care during their follow-up. There were no differences on MDI or PDI between cocaine exposed children placed in foster care compared to those in biologic maternal care (t values [$df = 1, 116$] ≤ 1.5, p values < .14).

Maternal Psychological Distress

There was a trend for mothers who were cocaine users during pregnancy to self-report greater severity of psychological distress symptoms in the postpartum period (Table 7).

Relationship of Drugs, Vocabulary, and Maternal Psychological Distress Symptoms to Outcomes

Relationships between maternal report of severity of use of various drugs and Bayley MDIs and PDIs at the oldest age are shown in Table 8. When amount and frequency of use were combined and averaged by trimester for the entire prenatal period, there were no relationships between any drug used and MDI. For PDI, there was one significant correlation (i.e., with the average amount of money spent on cocaine multiplied by frequency of use in the second trimester).

When amount and frequency of drug use were each calculated separately, however, additional significant relationships emerged for the MDI. There was a trend for number of days of use of cocaine per week for the month prior to pregnancy as well as the number of days per week of cocaine use for the second and third trimesters to be related to lower MDI scores. The number of days of alcohol use per week for the month prior to pregnancy was significantly related to lower MDI score, while there were trends for first, second, and third trimester use to also be related to lower MDI. No measure of tobacco or marijuana use was related to outcome, nor did any measure of alcohol use relate to PDI scores. Days per week of cocaine use in the third trimester was significantly correlated with lower PDI while

second trimester days of cocaine use and amount of money spent on cocaine were also weakly related to motor outcome.

Confounding variables

Pearson product moment correlations between overall maternal use of each drug and Bayley outcomes are presented in Table 9. Consistent with the findings from trimester use, maternal cocaine and alcohol use were significantly related to lower infant Bayley MDI scores, and maternal cocaine use was negatively related to PDI score as well. Neither marijuana nor tobacco use was related to outcomes and thus was not evaluated in regression analyses.

Maternal vocabulary score was unrelated to either MDI or PDI and was also dropped from the model. The summary score from the BSI (i.e., the General Severity Index [GSI] was strongly related to MDI ($r = -.34$, $p < .005$) but unrelated to PDI ($p > .20$). Thus, based on the criteria noted above for mediation, maternal distress was evaluated as a potential mediator of the effects of fetal cocaine exposure on MDI.

Effects of cocaine versus other drugs on outcome

To assess the relationship of cocaine relative to other drug exposures on outcome, two separate hierarchical multiple regressions were calculated (Table 10). For each, time of testing was entered on the first step as a control variable, followed by alcohol use, and then cocaine use. Neither tobacco nor marijuana were controlled for in these equations, since correlations had demonstrated that they were unrelated to either outcome measure (Tables 8, 9). These analyses indicated that cocaine and alcohol exposure had significant effects on MDI, after controlling for age at test. Cocaine's effects remained significant after control for alcohol exposure. For PDI, only cocaine exposure was a significant predictor.

Effects of maternal distress and drug exposure on outcome

To assess the effects of maternal distress on outcomes relative to the effects of drug exposure two additional regression equations were compared (Table 11). Each outcome variable (MDI or PDI score), was regressed first on age of child at Step 1 test because age at test had been shown to relate to MDI in the correlation analyses. Infant gestational age was controlled on Step 2 because of its relationship to prematurity in prior studies (Brooten et al., 1988; Singer, Davillier, Bruening, Hawkins, & Yamashita, 1996). The GSI scores, the summary distress measure from the BSI, was entered on the third step to assess the effects of severity of maternal psychological distress symptoms. This summary measure was followed by those drug exposures which showed significant relationships to either outcome in correlation analyses (alcohol and cocaine), entered as dichotomous (exposure/nonexposure) variables.

Based on Baron and Kenny's criteria, maternal psychological distress did not function as a mediator of cocaine's effects on mental outcome. Although correlated with cocaine status and mental outcome, cocaine remained a significant predictor of mental outcome after maternal distress was controlled in the regression equation. Thus, the effects of maternal distress are independent and additive to the developmental risk of cocaine exposure.

Because maternal distress did not mediate cocaine's effects, and because both cocaine exposure and distress were significant predictors of outcome, we then tested the potentially moderating effects of maternal distress with cocaine exposure on outcome. Moderator effects were evaluated by entering an interaction term (GSI × cocaine exposure) into the regression equation after GSI and cocaine exposure were entered separately. The interaction was not significant.

Infant prematurity level, maternal psychological distress, and alcohol exposure each predicted significant variance in infant mental outcome, with all three variables contributing to poorer MDI at follow-up. When all three variables were considered, cocaine retained a significant effect. Alcohol was not a significant predictor ($p < .20$), once cocaine exposure was considered. Severity of maternal psychological distress was also related to poorer MDI, even after control for all other drug use ($p < .003$).

Neither infant prematurity, maternal psychological distress, nor alcohol use was related to infant motor outcome. However, cocaine exposure was a significant predictor, even when all other variables were controlled ($p < .05$). For both mental and motor outcomes, after control for all other factors, cocaine exposure accounted for an 8–9 point lowering of standard score, exerting a medium effect size.

Discussion

Findings from the present study indicate that poor, urban, African-American children who were cocaine exposed in utero achieved lower scores on standard developmental assessments of mental and motor development during the second year of life, when compared to nonexposed children of similar race, age, and socioeconomic status. Differences persisted even when the higher incidence of prematurity in the cocaine exposed group was controlled and when severity of maternal psychological distress and other drug use were accounted for. Cocaine exposure was the best predictor of poorer mental and motor outcomes. Alcohol use was also a significant predictor of poorer mental outcome while neither marijuana nor tobacco use was related to either outcome. Although differences between groups are clinically significant, performance of the cocaine exposed group was still within the average range.

Severity of maternal psychological distress was also predictive of child mental, but not motor, outcome. The effects of maternal psychological distress remained significant, even when maternal cocaine use and use of all other drugs were controlled, indicating an independent negative effect of maternal distress symptoms on child mental development.

Our findings support previous studies in which global deficits in developmental outcome have been identified in cocaine and polydrug exposed cohorts in the second year of life (Chasnoff, Griffith, Freier, & Murray, 1992; Rodning, Beckwith, & Howard, 1989; Singer, Yamashita, Hawkins, Cairns, Baley, & Kliegman, 1994; Van Baar & De Graaf, 1994). These deficits were found in both cognitive and motor skills, suggesting a biologic impact of cocaine or polydrug exposure on child development, as gross motor skills are not as susceptible to social class or environmental influences as the language and problem solving

skills reflected in the MDI (Bendersky & Lewis, 1994; Singer, Yamashita, Lilien, Collin, & Baley, 1997).

Studies using animal models have reported decreased learning ability neonatally in rodents exposed to cocaine in utero (Heyser, Chen, Miller, Spear, & Spear, 1990; Heyser, Miller, Spear, & Spear, 1992; Spear et al., 1989), but not all studies have been confirmatory (Riley & Foss, 1991). Specific deficits in a contingency learning task were also identified at 4 and 8 months in cocaine exposed human infants (Alessandri, Sullivan, Imaizumi, & Lewis, 1993).

Higher risk for motor dysfunction in the first year of life has been a prominent, albeit not universal, finding from developmental studies of the effects of fetal cocaine exposure. Abnormal reflex development (Henderson & McMillen, 1990) has been identified in rodent models of fetal cocaine exposure, as well as in human neonatal studies (Coles, Platzman, Smith, James, & Falek, 1992; Neuspiel et al., 1991). Likewise, abnormalities in motor behaviors in cocaine exposed infants have been identified on the Movement Assessment of Infants at 4 and 12 months of life (Arendt, Angelopoulos, Bass, Mascia, & Singer, 1995; Arendt, Minnes, & Singer, 1996; Rose–Jacobs, Frank, Brown, Cabral, & Zuckerman, 1994; Schneider & Chasnoff, 1987). Relatively poorer motor skills were also found in 3-month-old cocaine exposed infants on the Bayley Motor Scale, but not after accounting for the effects of other drugs (Mayes, Bornstein, Chawarska, & Granger, 1995).

Several differences in design and methodology may have enhanced this study's power to detect differences between cocaine and noncocaine exposed infants on global scales of infant development. First, of currently reported prospective follow-up studies, only two have followed children into the second year of life. Of these, Chasnoff's cohorts were comprised of infants whose mothers entered drug treatment programs in pregnancy and whose children were also seen for developmental interventions. These treatment programs differentiated them from mothers in this study, the majority of whom had few options for treatment while pregnant during the time of enrollment in the study. Thus, infants in the present study may have had greater exposure and may be more generalizable to the broader population of cocaine exposed infants. In contrast to other studies, mothers in the control group were required to be negative for cocaine use on both a biologic measure and an extensive clinical interview, decreasing the chance that mothers in the control group were misclassified, and increasing the study's power to detect differences. It is more difficult, however, to account for the differences between the present study and that of Hurt and colleagues (Hurt et al., 1995), since the subject populations studied are remarkably similar in recruitment criteria, retention rates, maternal drug treatment status, and birth and outcome characteristics.

Poorer cognitive and motor outcomes are consistent with cocaine's known actions on neurotransmitter systems during fetal growth, which may interfere with neuronal development (Cregler and Mark, 1986; Volpe, 1992). Cocaine may also indirectly affect cognitive and motor functions through several other mechanisms, including vascular disruption leading to uterine hypoxia (Wood, Plessinger, & Clark, 1989), nutritional deficits associated with fetal growth retardation (Frank et al., 1990; Hadeed & Siegal, 1989; Lester et al., 1991; Singer, Arendt, Song, Warshawsky, & Kliegman, 1994; Zuckerman et al.,

1989), and an increased incidence of subtle brain lesions (Chasnoff, Bussey, Savic, & Stack, 1986; Frank, McCarten, Cabral, Levinson, & Zuckerman, 1994; Singer et al., 1994).

Effects of alcohol exposure were also found on mental developmental outcome, consistent with many prior reports (Brown et al., 1991; Jacobson et al., 1993; Streissguth, 1986a, 1986b). In the present study, independent effects of alcohol were not found once cocaine use was controlled. However, the research design was not geared towards evaluating the effects of individual drugs. Moreover, all cocaine exposed infants were polydrug exposed, leaving open the possibility that a combination of drug exposures is responsible for the long-term effects.

Of significance for teratologic studies is that several specific dose–response relationships were found between maternal reports of severity and quantity of drug use and developmental outcomes. Maternal report of frequency of days of cocaine use in the second and third trimester had a low, but significant, inverse relationship to MDI, as did a summary score combining frequency of cocaine use with amount reported in the second trimester. A dose–response relationship was also found between frequency of alcohol use in the month prior to pregnancy and MDI score, while similar trends were apparent for frequency use for all three trimesters. The association of maternal report of level of alcohol use prior to pregnancy has been previously reported (Streissguth, Barr, Martin, & Herman, 1980), and may reflect maternal likelihood of more accurate report of drinking patterns when questions are not linked to the known risks on offspring of alcohol use during pregnancy.

Perhaps more importantly, higher rates of various psychiatric disorders and disturbed patterns of relatedness have been noted in studies of substance abusing women (Fullilove et al., 1993; Griffin, Weiss, Mirin, & Lange, 1989). In particular, depression, anxiety, posttraumatic stress disorder, and personality disorders have been prominent. In a prior report on the mothers described in the present study, the greater severity of general distress symptoms found in the cocaine using group reflected clinically relevant symptoms of phobic anxiety and paranoid ideation (Singer, Farkas, Arendt, Minnes, Yamashita, & Kleigman, 1995). Such symptoms are key features of posttraumatic stress disorder, which may occur in elevated rates in addicted women, and are consistent with the growing evidence of history of sexual and violent physical trauma in women seeking treatment (Fullilove et al., 1993; Grice, Brady, Dristan, Malcomb, & Kilpatrick, 1995). Other studies have implicated depressive affect as particularly salient for cocaine using women (Weiss, Griffin, & Mirin, 1989; Woods, Eyler, Behnke, & Conlon, 1993).

Given the central role of the primary care-giver, usually the mother, in fostering the emotional and cognitive environments of the infant, the relationship between severity of maternal psychological distress symptoms and mental outcome in the second year of life is not surprising. A primary task of infancy and early childhood is the establishment of social and emotional relationships with others (Ainsworth, 1973; Bowlby, 1969). Caregiver consistency, positive affect, and synchronous interactions contribute to the development of security of infant attachment and cognitive competence (Cicchetti and Toth, 1995; Cummings & Cicchetti, 1990; Field, 1995). In addition to a host of social risk factors associated with a drug using lifestyle, maternal psychological distress and the cognitive and

affective impairments associated with chronic drug use are likely to interfere with her ability to structure an adequately consistent, positive, and contingent caregiving relationship necessary for optimal development.

In the animal literature, cocaine treated rat dams were found to be more aggressive than nontreated dams (Heyser, Molina, & Spear, 1992). When non-cocaine exposed rat pups were reared by these treated dams in a surrogate fostering study, the pups also displayed more aggressive behavior, suggesting that these behavioral deviations were mediated by dam–pup interaction patterns rather than direct CNS effects (Goodwin, Heyser, Moody, & Rajachandrian, 1992).

To date, the relationship of impaired mother–child interactions to the cognitive and emotional outcomes of cocaine and other substance exposed populations have not been well studied. The extreme end of the continuum of dysfunctional parenting in substance abusing populations is apparent in the disproportionately high representation of substance using families among children in out-of-home placements due to child abuse or neglect (Rogosch, Cicchetti, Shields, & Toth, 1995), and in the extraordinarily high rate of foster care placement for infants of cocaine using mothers (Children's Defense Fund, 1990). Direct observations of mother–child interactions have suggested disturbed interpersonal relationships in cocaine exposed, mother–child dyads manifest through insecure and disorganized attachment behaviors (Rodning, Beckwith, & Howard, 1989). Greater comorbid maternal psychopathology, in the form of antisocial personality disorder symptomatology, has been related to poorer maternal child interactions in 2-year-old children whose mothers were on methadone maintenance in one report (Hans, Bernstein, & Henson, 1990). Our findings suggest that the higher rates of psychiatric disorders in substance using populations, occurring as predisposing factors for substance abuse or as sequelae of chronic drug abuse, may be causally related to poorer child behavioral and cognitive outcomes. The present study suggests that, because of the differential effects of maternal psychological distress on the mental and motor functions at outcome, maternal psychopathology must be considered as an additional factor contributing to poorer cognitive competence in cocaine exposed populations.

Several limitations to the present study should be considered. Only urine screens were available as a biologic measure. Thus, some mothers in the control group who had used cocaine earlier in their pregnancies could have been categorized incorrectly, increasing chances of Type II error. This would have been a concern, however, only if differences were not apparent between groups. Another issue is that examiners were not blinded to cocaine status because developmental assessments were conducted as part of a clinical program. Lack of blinding may bias examiners to rate cocaine exposed children less favorably. Examiners were blinded to maternal psychological distress, however, and the differential effects of maternal distress, gestational age, and alcohol exposure on outcomes, despite their association with cocaine use, suggests the validity of these findings. Finally, while a number of important variables known to impact on child outcomes were considered in this paper, other factors important to outcome were not available (e.g., maternal perception of social supports, education, level of violence in the home, and maternal participation in drug treatment). The key constructs evaluated, however (i.e., maternal distress, cocaine, and

polydrug exposure, and child mental and motor outcomes), have not been previously evaluated in terms of their relationships to each other and to long-term outcomes.

Further studies are needed on the parenting capacities and interactions of cocaine using women, as well as on the type and severity of psychological disorders concomitant with, or predisposing to, maternal drug usage. Continued assessment of specific domains of child development which might be differentially vulnerable to prenatal drug exposure can help in understanding how specific biologic vulnerabilities interact with environmental factors, such as parenting behaviors and maternal psychopathology, to affect child outcome.

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Table 1

Demographic characteristics

Characteristics	Cocaine (*n* = 160)	Noncocaine (*n* = 56)	χ^2	*p*
Mother				
Race (% African American)	99	96	0.18	.67
Age (years)	28 ± 5	23 ± 4	5.4	< .0001
Prenatal care received	72%	84%	2.4	.13
Gravida	4.2 ± 2	3.3 ± 2	2.4	< .05
Tobacco use	83%	40%	22.2	< .001
Alcohol use	70%	42%	5.7	< .05
Marijuana use	45%	13%	12.3	< .001
PPVT standard score	79 ± 16	79 ± 12	0.03	< .96
Infant				
Gestational age (weeks)	38.1 ± 2	38.9 ± 2	1.8	< .07
Birth weight (g)[a]	2837 ± 467	2977 ± 503	0.85	.40
Birth length (cm)[a]	47.8 ± 3	48.5 ± 2	0.51	.61
Head circumference (cm)[a]	33.1 ± 2	33.6 ± 2	0.66	.51
Gender (% female)	51 ± 114	13 ± 33	2.6	.11

[a] *p*s adjusted for gestational age.

Table 2

Maternal drug use history

	Age at First Use (Years)			
	Cocaine ***M* ± *SD***	**Noncocaine** ***M* ± *SD***	***t***	***p***
Cocaine	23.4 ± 5	20.2 ± 2[a]	2.6	<.05
Alcohol	16.1 ± 4	16.8 ± 4	.9	.33
Marijuana	15.8 ± 3	16.6 ± 3	1.4	.19
Tobacco	15.5 ± 3	15.8 ± 5	1.5	.16
Duration of use (years)[b]				
Cocaine	4.7 ± 5	—	—	—
Alcohol	10.9 ± 5	6.1 ± 5	1.9	<.06
Marijuana	9.1 ± 5	4.7 ± 3	2.2	<.05
Tobacco	12.1 ± 6	7.9 ± 6	.4	.78

[a] For five women who had history of cocaine use prior to the month before pregnancy.

[b] Adjusted for maternal age.

Table 3

Frequencies and amounts of prenatal drug use by group

	Cocaine Positive (*n* = 123) *M* ± *SD*	Cocaine Negative (*n* = 50) *M* ± *SD*	*t*	*p*
Cigarettes/day				
Month prior	9.1 ± 9	5.2 ± 13	1.9	<.07
Trimester 1	9.2 ± 11	5.0 ± 13	2.1	<.05
Trimester 2	9.0 ± 10	5.0 ± 13	1.9	<.06
Trimester 3	9.0 ± 10	4.6 ± 13	2.1	<.05
Alcohol drinks/day				
Months prior	1.1 ± 1	0.3 ± 0.6	534	<.0001
Trimester 1	0.9 ± 1	0.4 ± 0.8	3.8	<.001
Trimester 2	0.0 ± 1	0.2 ± 0.5	5.7	<.0001
Trimester 3	0.8 ± 1	0.1 ± 0.5	5.9	<.0001
Alcohol days/week				
Months prior	2.3 ± 2	0.6 ± 2	5.9	<.0001
Trimester 1	2.1 ± 2	0.6 ± 1	5.2	<.0001
Trimester 2	1.9 ± 2	0.3 ± 1	5.9	<.0001
Trimester 3	1.7 ± 2	0.3 ± 1	5.7	<.0001
Joints/day				
Month prior	0.4 ± 0.9	0.08 ± 0.3	3.7	<.001
Trimester 1	0.3 ± 0.8	0.03 ± 0.2	4.1	<.0001
Trimester 2	0.3 ± 0.6	0.05 ± 0.2	3.9	<.001
Trimester 3	0.5 ± 0.8	0.06 ± 0.2	4.7	<.0001
Marijuana days/week				
Month prior	1.1 ± 2	0.2 ± 0.8	4.5	<.0001
Trimester 1	0.9 ± 2	0.3 ± 0.1	3.0	<.005
Trimester 2	0.8 ± 2	0.1 ± 0.7	4.0	<.0001
Trimester 3	1.0 ± 2	0.2 ± 0.8	4.3	<.0001

Table 4

Frequency and amounts of cocaine use by trimester

	Cocaine Positive (*n* = 123) *M* ± *SD*
Cocaine number rocks	
Month prior	2.2 ± 4
Trimester 1	1.5 ± 2
Trimester 2	2.0 ± 6
Trimester 3	1.7 ± 2
Cocaine days/week	
Month prior	2.6 ± 3
Trimester 1	2.4 ± 2
Trimester 2	2.2 ± 2
Trimester 3	2.5 ± 2
Cocaine cost	
Month prior	$54 ± $111
Trimester 1	$51 ± $84
Trimester 2	$38 ± $76
Trimester 3	$40 ± $60

Table 5

Summary variables of average prenatal drug use by group

	Cocaine Positive (*n* = 123) *M* ± *SD*	Cocaine Negative (*n* = 50) *M* ± *SD*	*t*	*p*
No. cigarettes/day total	10 ± 12	3 ± 5	4.9	<.0001
Alcohol use[a]				
Month prior	3.0 ± 6	0.3 ± 1	4.7	<.0001
Trimester 1	2.3 ± 5	0.3 ± 1	4.3	<.0001
Trimester 2	2.0 ± 5	0.1 ± 2	4.4	<.0001
Trimester 3	1.7 ± 4	0.1 ± 4	4.0	<.0001
Total	2.3 ± 5	0.2 ± 0.6	4.7	<.0001
Marijuana use[b]				
Month prior	0.9 ± 3	0.05 ± 0.3	2.9	<.005
Trimester 1	0.7 ± 3	0.04 ± 0.3	2.7	<.005
Trimester 2	0.5 ± 2	0.04 ± 0.3	2.3	<.05
Trimester 3	0.7 ± 3	0.05 ± 0.3	2.6	<.01
Total	0.7 ± 2	0.04 ± 0.3	2.6	<.005
Cocaine use[c]				
Month prior	3.8 ± 17			
Trimester 1	1.8 ± 5			
Trimester 2	2.0 ± 9			
Trimester 3	1.2 ± 3			
Total	2.6 ± 8			

[a]Number of drinks/day × number of days/week.

[b]Number of joints/day × number of days/week.

[c]Number of rocks/day × number of days/week.

Table 6

Group differences on Bayley mental and motor scores

Variable	Cocaine *M* ± *SD*	Noncocaine *M* ± *SD*	*t*	*p*
Chronologic age (months)	17.1 ± 9	16.4 ± 8	0.5	.62
Corrected age (months)	16.9 ± 9	16.2 ± 8	0.2	.90
Mental development index[a]	94.4 ± 17	102.5 ± 16**	4.7	< .05
Psychomotor index[a]	101.2 ± 16	108.0 ± 12*	4.0	< .05

[a] *p*s adjusted for gestational age.

** $p < .01$;

* $p < .05$.

Table 7

Brief Symptom Inventory and PPVT scores

Variable	Cocaine	Noncocaine	*t*	*p*
General severity index	0.52 ± 0.5	0.42 ± 0.4	1.5	<.10*
PPVT standard score	79 ± 16	79 ± 12	0.03	<.96

* *p* one-tailed.

Table 8

Correlations of drug use and outcomes (n = 90)

	MDI	PDI
Days/week cocaine use		
Month prior	−.19*	−.14*
First trimester	−.14	−.06
Second trimester	−.22**	−.18*
Third trimester	−.24**	−.21**
Cocaine cost		
Month prior	−.07	−.10
First trimester	−.05	.02
Second trimester	−.18*	−.22*
Third trimester	−.21*	−.14
Days/week marijuana use		
Month prior	−.16	−.09
First trimester	−.17	−.11
Second trimester	−.17	−.09
Third trimester	−.12	−.08
Number of cigarettes/day		
Month prior	−.01	−.01
First trimester	−.01	−.01
Second trimester	−.02	−.01
Third trimester	−.02	−.01
Number of drinks/day		
Month prior	−.19*	.01
First trimester	−.10	−.06
Second trimester	−.15	−.01
Third trimester	−.11	.03
Days/week alcohol use		
Month prior	−.24**	−.11
First trimester	−.19*	−.06
Second trimester	−.18*	−.06
Third trimester	−.18*	−.04

** $p < .05$;

* $p < 10$.

Table 9

Correlations between maternal drug use and child outcome

	MDI	PDI
Cocaine	−.24**	−.19*
Alcohol	−.21*	.02
Marijuana	−.14	.02
Tobacco	−.15	−.09

** $p < .001$;

* $p < .05$.

Table 10

Multiple regressions to assess the effects of substance use on outcome

Variable	B^a	β	R^2 Change	*p*
Criterion: MDI				
Step 1: age at test	−4.2	−.30	.09	< .0002
Step 2: alcohol use	−7.3	−.21	.01	< .05
Step 3: cocaine use	−8.7	−.24	.06	< .02
Criterion: PDI				
Step 1: age at test	0.30	.03	—	< .76
Step 2: alcohol use	−0.44	.02	—	< .89
Step 3: cocaine use	−9.0	−.29	.08	< .01

[a]Unstandardized regression coefficient.

Table 11

Summary of hierarchical regression analyses for variables predicting MDI and PDI scores

Variable	B^a	β	R^2 Change	*p*
Criterion: MDI				
Step 1: age at testing	−4.2	−.30	.00	<.002
Step 2: gestational age	−1.1	−.13	.02	<.09
Step 3: general severity index	−10.6	−.26	.04	<.03
Step 4: alcohol use	−7.3	−.20	.10	<.08
Step 5: cocaine use	−9.3	−.25	.05	<.05
Criterion: PDI				
Step 1: age at testing	0.30	.02	—	.76
Step 2: gestational age	−0.46	.03	—	.73
Step 3: general severity index	−0.13	−.14	.04	.26
Step 4: alcohol use	0.4	.04	—	.69
Step 5: cocaine use	−8.4	−.27	.08	<.05

[a]Unstandardized regression coefficient.