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Prenatal Cocaine Exposure and Children's Language Functioning at 6 and 9.5 Years: Moderating Effects of Child Age, Birthweight, and Gender

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Abstract

Objective—To evaluate whether prenatal cocaine exposure (PCE), or the interaction between PCE and contextual variables, is associated with children's language at age 6 and 9.5 years, adjusting for relevant covariates.

Methods—Analyses were based on 160 low-income, urban children from a prospective study who completed a standardized language assessment at 6 and 9.5 years. PCE was determined using neonatal meconium assays and maternal self-report.

Results—Significant interaction effects of PCE on language outcomes were found in multivariate longitudinal analyses using generalized estimating equations (GEE). Children with PCE had lower receptive language than unexposed children at 6 but not at 9.5 years, lower expressive language if they had lower birthweight, and lower expressive and total language if they were female. Other risk (e.g., violence exposure) and protective factors (e.g., preschool experience) were related to language outcomes regardless of PCE status.

Conclusions—Age, birthweight, and gender moderated the relation between PCE and school-aged children's language.

Keywords

birthweight; elementary school-aged children; gender; prenatal cocaine exposure; preschool experience; receptive and expressive language development; violence exposure

Whether prenatal cocaine exposure (PCE) is related to decrements in children's language during the elementary school years has not been established. Language is a critical component of school-aged children's successful academic and socio-emotional functioning (Rutter & Mawhood, 1991). Expressive language delays have been linked to poorer social competence (Horwitz et al., 2003) and, in some studies, behavior problems (Caulfield, Fischel, DeBaryshe, & Whitehurst, 1989).

Most studies evaluating the relation between PCE and language have focused on toddlers and preschoolers, and results have been inconsistent. In several large covariate-controlled prospective studies (Hurt, Malmud, Betancourt, Brodsky, & Giannetta, 1997; Kilbride, Castor, Hoffman, & Fuger, 2000), no significant effects of PCE on language were found. Similarly, in prior research with the present cohort, no significant PCE effects were found on standardized measures of receptive or expressive language or on general measures of language maturity (utterance complexity, vocabulary types) derived from transcripts of spontaneous language at age 2 (Beeghly et al., 1996), or on verbal ability (verbal IQ) assessed with the Wechsler Preschool and Primary Scales of Intelligence (WPPSI-R) (Wechsler, 1989) at age 4 (Frank et al., 2005).

In other large covariate-controlled prospective studies, significant PCE-related decrements in children's language functioning were reported, although specific findings vary. Singer et al. (2001) found that one-year-olds with heavier PCE had lower standard scores for auditory comprehension (receptive language) than unexposed infants, and lower total language scores than infants with either lighter PCE or no PCE. In a follow-up of this sample at age 4 (Lewis et al., 2004), PCE was related to poorer expressive and total language scores, but not receptive language scores, although children with PCE were more likely to have mild delays in receptive language. Morrow et al. (2003) found a significant effect of PCE (mediated by fetal growth) on children's aggregated total language standard scores at 4, 8, 12, 18, and 24 months using generalized estimating equations (GEE). In a later analysis of expressive and receptive language scores in the same sample at 36 months, heavier PCE was associated with lower expressive (but not receptive) language scores (Morrow et al., 2004). Although this finding remained significant after adjustment for children's fetal growth, prenatal exposure to other substances, gender, age at test, 3-year IQ, and maternal age, it was reduced to marginal significance ($p = .06$) after the caregiver's education and paternal involvement were added to the model, highlighting the importance of evaluating caregiving factors in behavioral teratology research with children.

In smaller studies with heterogeneous samples and methods, conflicting results have been reported. In several studies, no significant PCE effects were found (Espy, Kaufmann, & Glisky, 1999; Hawley, Halle, Drasin, & Thomas, 1995; Phelps & Cottone, 1999) whereas in other studies significant PCE effects on standardized language scores (receptive, expressive, or both) were reported (Bender et al., 1995; Chapman, 2000; Johnson, Seikel, Madison, Foose, & Rinard, 1997; Nulman et al., 2001). However, prenatal exposure to other substances was not always controlled.

Only a few prospective studies have evaluated the relation between PCE and language beyond the preschool period. Delaney-Black et al. (2000) found no significant effects of PCE on measures of six-year-olds' expressive language assessed using either standardized tests or language samples, in either bivariate or multivariate analyses. However, when vocabulary-based "low language" subgroups were created, children with PCE were more than twice as likely as unexposed children to be classified in the low language group. Prenatal nicotine exposure was also related to delayed language in this study. Bandstra et al. (2002) found a significant PCE effect on children's total language scores at 3, 5, and 7 years of age using longitudinal GEE analyses, controlling for relevant covariates. In a later analysis of these data, heavier PCE was also related to lower total language scores (Bandstra, Vogel, Morrow, Xue, & Anthony, 2004).

Consistent with recent theoretical work emphasizing the importance of evaluating contextual factors in substance abuse research (Cicchetti & Luthar, 1999; Institute of Medicine, 1996; Neuspiel, 1995), most of the prospective studies reviewed above found that child gender and other risk and protective factors (e.g., birthweight, caregivers' education, verbal ability, home

environment, and custody arrangements) were significantly related to children's language outcomes, regardless of their PCE status. Although less consistently evaluated, significant mediating or moderating effects have also been reported. In one prospective study, measures of fetal growth (e.g., birthweight) mediated the relation between PCE and total language scores in early childhood (Morrow et al., 2003) but not at later ages (3–7 years) (Bandstra et al., 2002). In both animal (Spear, Silveri, Katovic, Campbell, & Douglas, 2002) and human studies (Bennett, Bendersky, & Lewis, 2002; Delaney-Black et al., 2004), gender moderated PCE effects on developmental or behavioral outcomes. In other research, verbal scores were higher when children with PCE received case-managed versus routine-managed care, suggesting that environmental factors moderate PCE effects on children's verbal skills (Kilbride et al., 2000). Similarly, in prior studies with the present cohort, significant interactions of PCE with contextual factors (i.e., children's birthweight, custody arrangements, early intervention, birth mothers' parity, and public assistance) were observed for children's developmental and behavioral outcomes during early childhood (Beeghly, Frank, Rose-Jacobs, Cabral, & Tronick, 2003; Frank et al., 2002).

To date, no published prospective cohort study has evaluated the relation of PCE to standardized measures of children's receptive, expressive, and total language skills beyond the age of seven, when academic demands on language comprehension and production increase. This research is needed because PCE is hypothesized to affect areas of the brain associated with complex neurodevelopmental processes including language that cannot be reliably measured until school-age (Frank, Augustyn, Knight, Pell, & Zuckerman, 2001; Mayes, 1999).

The aim of the present analysis was to evaluate whether PCE, or the interaction between PCE and child age, gender, or other contextual variables, was independently associated with children's receptive or expressive language at 6 and 9.5 years of age, after controlling for relevant covariates. Based on a cumulative risk perspective (Sameroff, Seifer, Baldwin, & Baldwin, 1993), the researchers expected that contextual risk factors (e.g., lower birthweight) would mediate or moderate any PCE effects on language found, such that exposed children with other elevated risks would have lower language scores.

Method

Analyses in the present study were based on language data collected at the 6 and 9.5-year visits in a prospective study evaluating the effects of level of PCE on children's growth and development from birth to 11 years of age. All study children were born at Boston City Hospital (now Boston Medical Center) and were from low-income, urban backgrounds. The Human Studies Committees of Boston City Hospital and Boston University School of Medicine approved the study. All birth mothers or other caregivers gave written informed consent. Beginning at the 8.5-year visit, the study children also provided written assent. In addition, a writ of confidentiality was obtained from the federal government to protect participants from having research data subpoenaed.

Recruitment and Inclusion Criteria

Infant-caregiver dyads were recruited on a daily basis from the postpartum floor of Boston City Hospital from October 1990 to March 1993 if they met the following inclusion criteria: infant gestational age ≥ 36 weeks, no obvious major congenital malformations, no requirement for neonatal intensive (NICU) care, no diagnosis of fetal alcohol syndrome in the neonatal record, and no indication (either by neonatal or maternal urine toxic screen or meconium assay or by history in medical record) of prenatal exposure to illegal opiates, methadone, amphetamines, phencyclidine, barbiturates, or hallucinogens, and no history of HIV seropositivity noted in the infant's or mother's medical record. In addition, mothers had to be

at least 18 years old and fluent in English. These criteria excluded subjects with known major risk factors (e.g., premature birth) that might confound any specific effects of PCE on child outcomes. English fluency was required because the neuropsychological measures planned for this cohort at older ages were not standardized for non-English speakers. Further details about recruitment procedures and sample characteristics are reported elsewhere (Frank et al., 1999).

Classification of PCE

Research staff interviewed study mothers at intake immediately postpartum about their pregnancy and lifetime use of cigarettes, alcohol, and illicit drugs using an adaptation of the fifth edition of the Addiction Severity Index (ASI) (McLellan et al., 1992). At least one biological marker (maternal or infant urine, or infant meconium) was obtained for each recruited dyad to confirm maternal self-reported exposure status. Urine samples were analyzed for benzoylecognine, opiates, amphetamines, benzodiazepines, and cannabinoids by radioimmunoassay using commercial kits (Abuscreen RIA, Roche Diagnostics Systems, Inc., Montclair, NJ). We also sought to collect meconium specimens from all enrolled infants for analysis by radioimmunoassay for the presence of benzoylecognine, opiates, amphetamines, benzodiazepines, and cannabinoids, using a modification of Ostrea's method (Ostrea, Brady, Parks, Asenio, & Naluz, 1989).

On the basis of composite information derived from maternal self-report and the meconium assays, subjects with PCE were further classified as either heavier or lighter exposed. "Heavier" use was defined a priori as the top quartile of days of self-reported use during the entire pregnancy and/or the top quartile of concentration for cocaine metabolites in the infant's meconium. The mean days of maternal self-reported cocaine use during pregnancy in this cohort was 20.6 days (range = 0–264); mothers reporting 61 or more days of cocaine use during pregnancy fell into the top quartile and were considered "heavier" users. The mean meconium concentration was 1143 ng of benzoylecognine per gram of meconium (range = 0–17,950 ng); infants with more than 3314 ng of benzoylecognine per gram of meconium were in the top quartile and were classified into the "heavier" group. All other PCE was classified as "lighter."

A classification system based on both self-report and meconium assay was used because 13.7% of the infants in the present sample (13.9% in the larger study) had no meconium assay. Mothers in the top quartile for self-reported use were classified as heavier users, even if the benzoylecognine level in their infant's meconium was not in the top quartile or if the infant's meconium assay was missing. This procedure was used because women are more likely to underreport than overreport illicit substance use during pregnancy (Ostrea, Brady, Gause, Raymundo, & Stevens, 1992) and because not all infants with PCE have positive meconium assays (Lester et al., 2001).

This ordinal classification scheme is similar to that used by other investigators of prenatal substance exposure (Alessandri, Bendersky, & Lewis, 1998; Jacobson, Jacobson, Sokol, Martier, & Chiodo, 1996; Singer et al., 2004). Prior research in the present cohort indicated that level of PCE defined this way was significantly related in a dose-related manner to lower birthweight *z*-scores (adjusted for gestational age and gender) (Frank, Augustyn, & Zuckerman, 1998), neonatal ultrasound findings (Frank et al., 1999), and less optimal patterns of newborn neurobehavior (Tronick, Frank, Cabral, Mirochnick, & Zuckerman, 1996). For consistency with previous work in this cohort, both a dichotomous PCE variable (unexposed/exposed) and an ordinal PCE variable (unexposed, lighter, heavier) as defined above were used in the statistical analyses.

Language Measures

Children's receptive, expressive, and overall (total) language functioning was evaluated using the Test of Language Development-Primary—Third edition (TOLD-P:3)(Newcomer & Hammill, 1997) at the 6-year visit and the Child Evaluation of Language Fundamentals—Third edition (CELF-3) (Semel, Wiig, & Secord, 1995) at the 9.5-year visit. Examiners at each age were masked to children's PCE status, background variables, and scores on prior developmental assessments. All children passed vision and hearing screens prior to testing.

The TOLD-P:3 (for ages 4–8 years, 11 months) and the CELF-R (for ages 6–21 years) were chosen because they are psychometrically sound, were recently renormed on nationally representative samples, and were shown to be unbiased relative to gender and race/ethnicity (Newcomer & Hammill, 1997; Semel et al., 1995). Moreover, the composite language standard scores derived from these instruments are moderately correlated with school achievement (Newcomer & Hammill, 1997; Semel et al., 1995).

Three composite standard scores (receptive language, expressive language, and total language) derived from each instrument served as the dependent variables in the longitudinal analyses described below. Each was standardized to have a mean of 100 and standard deviation of 15. On the TOLD-P:3, *receptive language* was derived from children's scores on two receptive subtests (Picture Vocabulary and Grammatical Understanding), *expressive language* from scores on four expressive subtests (Oral Vocabulary, Relational Vocabulary, Grammatical Completion, and Sentence Imitation), and *total language* from scores on all six subtests. On the CELF-R, *receptive language* was derived from children's scores on three receptive subtests (Concepts and Directions, Word Classes, and Semantic Relationships), *expressive language* from scores on three expressive subtests (Formulated Sentences, Recalling Sentences, and Sentence Assembly), and *total language* from scores from all six subtests. Although derived from the receptive and expressive language scores, total language was included as a dependent variable in this study to permit comparisons with other PCE studies using this variable (Bandstra et al., 2002).

Potential Control Variables

Potential control variables identified on theoretical grounds (e.g., child anthropometrics, health, gender, demographics, caregiver, and other environmental factors) were documented at intake and at each subsequent visit via medical record review, caregiver interviews, or direct child or caregiver assessment. The specific variables that were evaluated as potential covariates in the present study are listed in Tables I and II. These variables were chosen because they have been associated with PCE and/or with children's language or cognitive outcomes in prior research with this cohort or in other studies.

Both fixed (time-invariant) and time-dependent (assessed at the time of the 6 and 9.5-year visits) variables were evaluated. Fixed variables included birth mothers' race/ethnicity (African American/Caribbean versus other), age, education, parity, U.S.-born status, prenatal use of tobacco, alcohol, and marijuana (Bendersky, Alessandri, Gilbert, & Lewis, 1996; Frank et al., 2002; Singer et al., 2004), current caregivers' verbal ability (Lewis et al., 2004), children's gender (Beeghly et al., 1996; Morrow et al., 2003; Singer et al., 2001), birthweight z-score (adjusted for gestational age and gender, based on norms calculated from data compiled by the National Center for Health Statistics for natality in the United States in 1991) (National Center for Health Statistics, 1993), otitis-prone status (3 or more otitis media events through age two) (Black & Sonnenschein, 1993; Feldman et al., 2003), maximum whole blood lead values through age 4 (Bellinger, Stiles, & Needleman, 1992; Chiodo, Jacobson, & Jacobson, 2004), receipt of child-focused early intervention services through age 2 (Claussen, Scott, Mundy, & Katz, 2004; Frank et al., 2002), and preschool experience (e.g., Head Start) (Frank et al.,

2004). To control for the possible confounding effect of children's general nonverbal intelligence (Bandstra et al., 2004; Lewis et al., 2004), children's WPPSI-R performance IQ at age 4 was also evaluated. Caregivers' verbal ability was assessed using the Vocabulary standard score from the Kaufman Brief Intelligence Test (K-BIT) (Kaufman & Kaufman, 1990) measured at the 6-year visit. If a caregiver's K-BIT score was missing, their Vocabulary standard score from the Peabody Picture Vocabulary Test (PPVT-R) (Dunn, 1981) at intake was substituted. In validity studies (Dunn, 1981; Kaufman & Kaufman, 1990), the K-BIT and PPVT-R Vocabulary standard scores were highly correlated with Wechsler Verbal IQ ($r = .60$ and $.73$, respectively).

Potential time-dependent control variables included the child's current caregiver (birth mother, kinship caregiver, or nonkin foster caregiver) (Brown, Bakeman, Coles, Platzman, & Lynch, 2004; Frank et al., 2002; Lewis et al., 2004), current caregivers' education (Lewis et al., 2004; Morrow et al., 2003; Singer et al., 2004), marital status, employment status, public assistance (Bendersky et al., 1996), household size (number of adults and children) (Evans, Maxwell, & Hart, 1999), caregivers' current substance use (Griffith, Azuma, & Chasnoff, 1994), homelessness (any nights in a homeless shelter) (Bassuk, Weinreb, Dawson, Perloff, & Buckner, 1997), psychosocial adaptation (i.e., self-reported functional social support and psychological distress) (Lewis et al., 2004), and exposure to violence or victimization (caregiver or child) (Beeghly & Cicchetti, 1994; Koenan, Moffitt, Caspi, Taylor, & Purcell, 2003; Morrel, Dubowitz, Kerr, & Black, 2003). Caregivers' functional support was assessed using Norbeck's Social Support Questionnaire—short form (Norbeck, Lindsey, & Carrieri, 1981), and psychological distress was assessed using the Global Severity Index (GSI) of the Brief Symptom Inventory (BSI) (Derogatis & Spencer, 1982). Exposure to violence or victimization (child or caregiver) was evaluated via caregiver report using the Exposure to Violence Inventory (EVI) (Augustyn, Frank, Posner, & Zuckerman, 2002).

Statistical Analyses and Covariate Selection

The correlations between comparable language variables at each visit (e.g., receptive language at 6 and 9.5 years, expressive language at 6 and 9.5 years, total language at 6 and 9.5 years) were evaluated using Pearson correlations.

The relation between PCE and the language outcomes at 6 and 9.5 years was evaluated using bivariate and multivariate analyses. PCE was coded both as a dichotomous variable (exposed/unexposed) and as an ordinal variable (unexposed, lighter, heavier), as defined above. In the bivariate analyses, one-way ANOVA, Tukey post hoc tests, and Cohen's d (effect size) were used for continuous language variables (composite and subscale scores), whereas chi square analyses (with odds ratios, and 95% confidence intervals, CI) were used to evaluate the percentage of children in each PCE group with and without a low language composite score [i.e., standard score <70 , more than two standard deviations (SD) below the population mean, a marker of clinical concern].

Longitudinal analyses were carried out using GEE. The GEE modeling procedures specify a within-subject correlation structure and maximize statistical power by allowing for the interdependency of observations within the error structure of the model and by permitting the use of all available data at each point. These models also allow for time-dependent covariates, such as children's foster placement, which may differ at each age.

An initial “base” GEE model was constructed first, which included only the PCE variable and children's age at the time of testing. A multivariate GEE model was then constructed separately for each language variable, to evaluate the longitudinal relation between PCE, or interaction of PCE and contextual variables, and language outcomes at 6 and 9.5 years, adjusting for relevant covariates.

Retention of covariates in the multivariate models was based on both theoretical and statistical considerations. In addition to the base-model variables (PCE and child age at test), all models included prenatal exposure to tobacco (natural log of mothers' average daily number of prenatal cigarettes), marijuana (any prenatal use based on positive results of urine assay, meconium assay, or self-report), and alcohol (natural log of the mothers' average daily volume of alcohol during the last 30 days of pregnancy) as covariates, because of their association with prenatal cocaine use (Lester et al., 2001). Maternal recall of daily volume of alcohol use during the past 30 days of pregnancy was used because it is less subject to recall bias than a comparable variable assessing use during the entire pregnancy; however, these two variables were highly correlated ($r = .80$) in this sample.

Other control variables (listed in Tables I and II) were evaluated for possible inclusion in the multivariate GEE models following the method of Mickey and Greenland (Mickey & Greenland, 1989). Each potential control variable was evaluated one-by-one in preliminary multivariate GEE models for each dependent variable. Any variable that changed the unadjusted parameter estimate (slope) for PCE and a particular outcome by 10% or more was retained as a covariate in that model. This approach provides the most valid estimate of the effect of the exposure of interest on outcome in behavioral teratology studies, such as this study; however, it does not identify which control variable, among those evaluated, is the strongest predictor of outcome (Mickey & Greenland, 1989).

Formal collinearity diagnostics (Belsey, Kuh, & Welsch, 1980) were carried out on the final main effects models. Caregivers' self-reported use of cocaine, tobacco, marijuana, or alcohol at 6 and 9.5 years was highly correlated with the child's prenatal exposure to these substances and could not be included in the multivariate GEE models. All possible 2-way interactions between PCE and the control variables were then evaluated for possible inclusion. All interactions significant at $p \leq .05$ were retained in the final model. To evaluate whether birthweight was a significant mediator of the relation between PCE and language outcomes, as in prior research (Morrow et al., 2003), separate GEE analyses were carried out with and without birthweight (Baron & Kenny, 1986).

Statistical values generated in the GEE analyses were adjusted for PCE and all other variables included in that model. Means and standard errors for any significant cocaine main or interaction effects were computed from the estimated model parameters, adjusting for all other variables in the model. Findings are noted as statistically significant using an alpha level of .05 (two-tailed).

Results

Sample Retention and Characteristics

Of the 252 children enrolled in the study at birth, 160 children (63.5%) completed a standardized language assessment at the 6-year visit, the 9.5-year visit, or both, and comprised the present sample. Of the 160, (75 unexposed, 57 with lighter PCE, 28 with heavier PCE), 84 (52.5%) were male. There was no evidence of differential attrition when the 160 children in the present sample were compared to the 92 nonparticipants on presence or level of PCE. The retained and not retained subjects did not differ significantly on prenatal exposure to marijuana, alcohol, or tobacco, gestational age, gender, birthweight z -scores, birth mother's age, education, marital status, parity, race/ethnicity, U.S.-born status, or public assistance at intake. Moreover, child participants and nonparticipants in the present sample did not differ significantly on WPPSI-R full scale, verbal, or performance IQ at age 4.

In Table I, descriptive statistics are provided for the sample's demographic, maternal, and caregiver characteristics in the three PCE groups. There were no significant group differences

for the birth mothers' race/ethnicity (89% were African American/Caribbean), parity (36% were primiparas), or education ($M = 11.6$ years). Compared with nonusers, mothers who used cocaine during pregnancy were significantly older, more likely to be U.S.-born, and more likely to have used tobacco, alcohol, and marijuana during pregnancy.

At the 6 and 9.5-year visits, children in both the lighter and heavier PCE groups were more likely than their unexposed counterparts to be in the custody of a caregiver other than their birth mother (either kinship or nonkin foster care). Nonkin foster caregivers had significantly more years of education ($M = 13.4$ years) than kinship caregivers ($M = 11.9$ years) or birth mothers ($M = 11.9$ years), $p = .002$. Caregivers in the heavier PCE group had marginally higher verbal ability and education at the 6-year visit and lower self-reported psychological distress (BSI GSI) at the 9.5-year visit, than caregivers in the lighter or unexposed groups. However, there were no significant differences by PCE group in caregivers' self-reported total functional social support, household size (number of children or adults in the household), or self-reported use of alcohol, marijuana, cocaine, or other illicit drugs at the 6- or 9.5-year visits. At the 6-year visit, caregivers of children with heavier PCE smoked significantly more cigarettes per day than caregivers of unexposed children.

At the 6-year visit, most caregivers in each group were receiving public assistance [Aid to Families with Dependent Children (AFDC) or food stamps] and a low percentage was employed. Caregivers of children with heavier PCE were marginally more likely to be receiving public assistance than the other caregivers. At the 9.5-year visit, which took place after the passage of federal welfare reform legislation, only about a fourth of caregivers in each group was receiving public assistance [now Transitional Assistance for Needy Families (TANF) or food stamps] and a higher percentage was employed. There were no significant group differences in public assistance at the 9.5-year visit, but caregivers in the unexposed group were more likely to be employed than caregivers in the two exposed groups.

In Table II, descriptive statistics are provided for the biologic and social characteristics of the children in the three PCE groups. Children with heavier PCE had significantly lower birthweight z -scores (adjusted for gestational age and gender) than children with lighter cocaine exposure, who in turn had lower birthweight z -scores than the unexposed children. Children with heavier or lighter PCE were less likely than unexposed children to be in contact with their father at the time of the 6-year visit. There were no significant differences by PCE group for child gender, age at the time of the 6 or 9.5-year visit, general intelligence prior to formal schooling (WPPSI-R IQ scores at age 4), receipt of child-focused early intervention services (birth to 2 years), preschool experience, current academic problems (receipt of special education services or grade retention at 6 or 9.5 years), or child health or social risk indices relevant to language development, including otitis media episodes through age 2, maximum blood lead level through age 4, children's or caregivers' exposure to violence or victimization, or homelessness at the time of the 6- or 9.5-year visits. Roughly half of the children or caregivers in each PCE group at each visit had been exposed to violence or victimized, and by the 9.5-year visit, a third of the children were experiencing academic problems, as indexed by the percentage receiving special education services or grade retention.

Cross-Visit Correlations Between Language Measures

The language dependent measures were significantly and substantially correlated across visits (receptive language at 6 and 9.5 years, $r(131) = 0.65$, $p < .0001$; expressive language at 6 and 9.5 years, $r(131) = 0.71$, $p < .0001$; total language at 6 and 9.5 years, $r(131) = 0.69$, $p < .0001$).

Bivariate Analyses Relating PCE to Language Outcomes

In Table III, descriptive statistics are provided for children's average receptive, expressive, and total language standard scores at the 6 and 9.5-year visits, and for the percentage of children in each group with a low language score (<70) at 6 and 9.5 years, as broken down by the two-category PCE variable (unexposed, exposed). There were no significant PCE effects on any language variable at either age. However, at the 6-year visit, children with PCE had marginally lower scores than the unexposed children on the composite receptive language score, with a small effect size (Cohen's $d = -0.24$). There also were no significant PCE effects on any receptive or expressive subscale scores (data not shown). Regardless of PCE status, children's mean language scores fell within the low-average range of ability, based on published age norms. Moreover, a higher percentage of children in each group had a low language score (particularly at the 9.5-year visit), compared to the 2.5% expected in a normal distribution.

When the ordinal PCE variable (unexposed, lighter, and heavier) was used in these analyses, no significant differences were found between the unexposed group and either of the two exposed groups on any language measure. However, at the 9.5-year visit, children in the lighter PCE group had significantly lower mean scores than children in the heavier PCE group on expressive language ($p = .046$), suggesting that level of PCE was not related to language in a dose-related manner.

Generalized Estimating Equations (GEE): Base Model

Analyses in the GEE base models were based on 160 subjects and 293 observations. Adjusting for child age, there were no significant main effects of PCE on any language measure. For receptive language, mean scores and standard errors (SE) in the unexposed and exposed groups were 91.06 ($SE = 1.81$) and 89.88 ($SE = 1.50$), respectively, with a difference estimate of -1.18 , Wald 95% $CI = -5.33, 2.97$, $Z = -0.56$, $p = .58$. For expressive language, the mean scores in the unexposed and exposed groups were 91.44 ($SE = 1.94$) and 90.36 ($SE = 1.41$), respectively, with a difference estimate of -1.09 , Wald 95% $CI = -5.80, 3.63$, $Z = -0.45$, $p = .65$. For total language, the mean scores in the unexposed and exposed groups were 90.36 ($SE = 1.85$) and 89.44 ($SE = 1.38$), with a difference estimate of -0.92 , Wald 95% $CI = -5.44, 3.60$, $Z = -0.41$, $p = .72$.

The parameter estimate for child age was significant in the base models for receptive language (effect estimate = -1.02 , Wald 95% $CI = -1.74, -0.31$, $p = .005$) and total language (effect estimate = -0.703 , Wald 95% $CI = -1.25, -0.149$, $p = .014$), indicating that these scores decreased from 6 to 9.5 years. In separate analyses, a PCE by age interaction term was evaluated for each language variable and failed to reach significance (p -values for receptive, expressive, and total language = .145, .858, and .533, respectively).

When the GEE base model analyses were repeated using the ordinal PCE variable (unexposed, lighter, heavier), there were no significant differences between the unexposed group and the two exposed groups on any language outcome. However, as in the bivariate analyses, children with lighter PCE had lower expressive language ($p = .01$) and total language ($p = .03$) scores than children with heavier PCE.

Generalized Estimating Equations (GEE): Multivariate Models

Analyses in each multivariate model were based on 160 subjects; however, the number of observations in each model (253, 251, and 250 for receptive, expressive, and total language, respectively) varied somewhat because of missing data associated with the specific variables included in different models. In addition to the base-model variables (PCE and child age at test), and other variables included a priori (prenatal exposure to tobacco, marijuana, and alcohol), the following control variables met criteria for inclusion in the models for all three

language variables (Mickey & Greenland, 1989): birth mothers' race/ethnicity and age at intake, the child's current caregiver (birth mother, kinship caregiver, and nonkin foster caregiver), caregivers' verbal ability and education, child's history of otitis media, early intervention services, preschool experience, and WPPSI-R Performance IQ score at age four.

Other variables were retained that were unique to the model for each dependent variable. In the model for receptive language, two additional covariates (caregivers' employment status and psychological distress) and a PCE by age interaction term were included. In the model for expressive language, four additional covariates (child gender, birthweight z-score, birth mothers' U.S.-born status, and child/caregiver exposure to violence or victimization) and two interaction terms (PCE by birthweight and PCE by gender) were included. In the model for total language, five additional covariates (child gender, birthweight, birth mothers' U.S.-born status, current caregivers' marital status, and child/caregiver violence exposure/victimization) and a PCE by gender interaction term were included. Results of formal collinearity diagnostics (Belsey et al., 1980) on the variables included in the main-effects models for each dependent variable indicated no presence of multi-collinearity.

When the multivariate GEE analyses were carried out using the dichotomous (unexposed/exposed) PCE variable, significant interactions of PCE with child contextual variables (age, birthweight, or gender) were found, adjusting for the influence of all other variables. In Table IV, the adjusted means and standard errors for these interactions, along with estimated difference scores, 95% confidence intervals, and *p*-values, are presented.

Receptive Language

A significant interaction of PCE with child age was found (type 3 $\chi^2 = 6.40$, $df = 2$, $p = .04$). Post hoc contrast analyses indicated that, at the 6-year visit, children in the unexposed group had significantly higher receptive language scores (by 6 points, on average) than children in the PCE group, but this difference diminished to non-significance at the 9.5-year visit.

Expressive Language

A significant PCE by birthweight interaction was found (type 3 $\chi^2 = 5.83$, $df = 1$, $p = .016$). Post hoc contrast analyses indicated that, at the 10th percentile for birth-weight, children with PCE had significantly lower expressive language scores (by nearly 8 points, on average) than unexposed children. In contrast, at the 50th percentile, the two groups did not differ significantly. The 10th percentile for birthweight was used as a risk marker in this study because it corresponds to the conventional cutoff used by clinicians for classifying "small for dates."

In addition, a significant PCE by gender interaction was found (type 3 $\chi^2 = 5.33$, $df = 1$, $p = .02$). Post hoc contrast analyses indicated that the expressive language scores of unexposed girls were significantly higher (by 9 points, on average) than those of girls with PCE, but boys' expressive language scores did not differ significantly by PCE status.

Total Language

A significant PCE by gender interaction was found for total language (type 3 $\chi^2 = 4.72$, $df = 1$, $p = .03$). Post hoc contrast analyses indicated that the total language scores of unexposed girls were significantly higher (by nearly 8 points, on average) than those of girls with PCE, but boys' total language scores did not differ significantly by PCE status.

Covariate Effects

Several significant covariate effects were observed for each dependent variable, adjusting for the effects of all other variables. Children had higher receptive, expressive, and total language scores if their current caregiver had higher verbal ability ($p = .02$, $.05$, $.03$, respectively), if

children had participated in a preschool enrichment program ($p = .003, .05, .02$, respectively), or if children had a higher WPPSI Performance IQ at age 4 (all p -values $< .001$). Children had higher receptive and total language and marginally higher expressive language scores if their birth mother was older at intake ($p = .01, .01, .06$, respectively). Moreover, children had higher expressive and total language scores if they or their caregivers had not been exposed to violence or victimized ($p = .001, .006$, respectively) or (paradoxically) if children had been exposed prenatally to cigarettes ($p = .02, .04$, respectively).

Several marginally significant covariate effects were also found. Children had slightly higher receptive language scores if they were in the custody of nonkin foster caregivers rather than their birth mothers or kinship caregivers at the time of testing ($p = .09$). In addition, children had marginally higher total language scores if their birth mother was an immigrant ($p = .07$).

Level of PCE

When the ordinal PCE variable (unexposed, lighter, heavier) was used in the multivariate GEE analyses, the PCE interaction effects for age and birthweight remained significant. At the 6-year visit, children in both the heavier and lighter PCE groups had significantly lower receptive language scores than unexposed children (difference heavier-unexposed = -7.77 , 95% $CI = -14.4, -0.15$, $p = .02$; difference lighter-unexposed = -5.08 , 95% $CI = -9.3, 0.9$, $p = .02$); however, at the 9.5-year visit, these differences were no longer significant. Similarly, at the 10th percentile for birthweight, children with lighter (but not heavier) PCE had significantly lower expressive language scores than unexposed children (lighter-unexposed difference = -10.47 , 95% $CI = -17.2, 3.8$, $p = .002$), but at the 50th percentile for birthweight, there were no significant group differences. The PCE by gender interaction term was not evaluated because it did not meet criteria for retention in the GEE multivariate models when the ordinal PCE variable was used.

Results of mediational analyses indicated that birthweight did not significantly mediate the relation between PCE and expressive or total language scores.

In separate analyses, the multivariate GEE analyses were repeated on a sample limited to children with complete language data at both ages. Results were very similar to those found in the full sample and are available upon request from the first author.

Discussion

This prospective cohort study is among the first to evaluate the relation between PCE and standardized measures of children's receptive and expressive language beyond the age of 7. Results from cross-sectional bivariate and longitudinal baseline GEE analyses controlling for age at testing (but no other covariates) revealed no significant main effects of PCE on any language measure at 6 or 9.5 years of age. Regardless of their PCE status, children's mean language scores (unadjusted or adjusted for covariates) were in the low-average range, based on published age norms, and a higher-than-expected percentage (based on a normal distribution) had a low language standard score (< 70), particularly at 9.5 years. These results mirror those found in this cohort at earlier ages (Beeghly et al., 1996; Frank et al., 2005) and in other prospective studies (Hurt et al., 1997; Kilbride et al., 2000) but contrast with the significant PCE effects on language reported in other prospective studies at school transition (Bandstra et al., 2002; Lewis et al., 2004).

Level of PCE also was not related to significant language differences between the unexposed group and the two exposed groups. However, prior to covariate control, children with lighter PCE had lower expressive and total language scores than children with heavier PCE, indicating that PCE was not related to these language outcomes in a dose-related manner. The latter

finding likely reflects differences in caregivers' characteristics (e.g., years of education, caregiver type) between the lighter and heavier PCE groups at this age period. Support for the validity of the 3-level PCE variable used in this study comes from prior infancy research with this cohort, wherein level of PCE defined in the same way was related in a dose-related manner to lower birthweight (Frank et al., 1998), neonatal ultrasound findings (Frank et al., 1999), and less optimal patterns of infant neurobehavior (Tronick et al., 1996).

As hypothesized in recent theoretical work on substance abuse (Cicchetti & Luthar, 1999; Institute of Medicine, 1996), significant interactions of PCE and child contextual variables (i.e., age, birthweight, and gender) emerged after covariate control, and specific findings varied depending on the type of language outcome (e.g., receptive versus expressive). Children in the unexposed group had significantly higher receptive language scores than children in either the lighter or heavier PCE groups at the 6-year visit but not at the 9.5-year visit. The decrease in scores for children in the unexposed group at 9.5 years may reflect the increased difficulty of the language comprehension items assessed at this age, which may have overwhelmed any PCE-related differences. Alternatively, this decline could be because of other differences in the two language assessments, although the composite language scores derived from each instrument were substantially correlated. Similar age-related declines for language (Fish & Pinkerman, 2003) and general cognitive functioning (Frank et al., 2002; Hurt et al., 1995; Messinger et al., 2004) have been reported for low-income children during early childhood but not, to our knowledge, during the elementary school years.

Consistent with a cumulative risk perspective (Beeghly & Tronick, 1994; Sameroff et al., 1993; Tronick & Beeghly, 1999), birthweight moderated (but did not mediate) the effect of PCE on children's expressive language in this sample. A similar finding was observed in an earlier analysis in this cohort, in which heavier PCE in interaction with birthweight at the 10th percentile was related to poorer psychomotor functioning during infancy (Frank et al., 2002). Possibly, subtle neurological differences related to early psychomotor functioning contributed to these children's lower expressive language scores at school age (Rose-Jacobs, Cabral, Beeghly, Brown, & Frank, 2004).

Gender moderated the effects of PCE on expressive language and total language scores, such that unexposed girls had higher scores than girls with PCE or boys in either PCE group. A similar trend was reported in a small sample of two-year-olds, in which girls whose caregivers used cocaine and other illicit substances had less complex expressive language (Malakoff, Mayes, Schottenfeld, & Howell, 1999). In other studies, boys with PCE exhibited greater vulnerability, as reflected in more teacher reported behavior problems at age 6 (Delaney-Black et al., 2004) and lower composite IQ scores at age 4 (Singer et al., 2004). Although the explanation for these contrasting findings is not known, they suggest that differing PCE effects on boys and girls may be domain-specific. Gender-specific PCE effects have also been reported in animal research and may reflect sex-related differences in brain morphology or metabolism (Spear et al., 2002).

Although intriguing, these PCE interaction effects emerged only after covariate control and should be interpreted with caution. Moreover, level of PCE was not related to language outcomes in a dose-related manner, suggesting that a simple toxicological model does not fully explain these findings.

Covariate Effects

Consistent with prior PCE research at school transition (Bandstra et al., 2002; Lewis et al., 2004), other risk and protective factors affected the language performance of children in this low-income cohort, regardless of their PCE status, and warrant further evaluation in future studies. A crucial and potentially modifiable social risk factor was violence exposure or

victimization, which affected approximately half of the sample. This variable was strongly and negatively related to children's expressive and total language functioning in both bivariate and multivariate analyses. This finding is consistent with prior research with younger children, in which violence exposure or victimization was related to delayed expressive language in toddlers (Beeghly & Cicchetti, 1994), poorer verbal abilities among preschoolers (Huth-Bocks, Levendosky, & Semel, 2001), delayed syntactic development at age 5 (Eigsti & Cicchetti, 2004), lower IQ at age 5 (Koenan et al., 2003), and increased behavior problems at 4 to 6 years (Morrel et al., 2003).

A finding with particular policy relevance was that children with or without PCE who had participated in preschool programs such as Head Start had more mature receptive and expressive language at school age than children who had not. A similar positive effect of preschool experience was found in this cohort for WPPSI-R IQ scores at age 4 (Frank et al., 2005). This present finding suggests that the positive benefits of preschool experience continue into the elementary school years.

Contrary to our expectations and prior reports (Fried, Watkinson, & Siegel, 1997; Richardson, Ryan, Willford, Day, & Goldschmidt, 2002), there were no significant effects of prenatal exposure to alcohol or marijuana, or significant interactions of these factors with PCE on children's language outcomes. Unexpectedly, and in contrast to other research (Delaney-Black et al., 2000), there was a significant paradoxical effect of prenatal cigarettes for children's expressive and total language scores. Although the explanation for this finding is unclear, a similar paradoxical finding was observed in this cohort for the relation between prenatal cigarette exposure and children's psychomotor functioning during infancy (Frank et al., 2002).

Limitations

The findings of this study were based on a sample of term or near term, predominantly African American/Caribbean children with and without PCE being raised in low income, urban neighborhoods. As a function of their participation in this study, these children received regular pediatric care and were referred on an as-needed basis to intervention services. The results of this study may not generalize to other groups of children, such as those exposed prenatally to other illicit drugs (e.g., opiates), those born prematurely or with serious comorbid health conditions, or those who have not experienced close monitoring by health care providers.

In addition, the primary analyses in this study were based on standardized receptive, expressive, and total language scores, rather than on qualitative measures of specific skills (e.g., pragmatics derived from language transcripts). Such measures have been related to PCE or caregivers' postnatal cocaine/polydrug use in prior research with young children (Bland-Stewart, Seymour, Beeghly, & Frank, 1998; Lewis et al., 2004; Malakoff et al., 1999; Mentis & Lundgren, 1995) and warrant further evaluation at school age in large prospective studies.

Clinical and Policy Implications

Consistent with findings from prior PCE research, the results of this study do not support early fears that PCE causes universal or profound developmental problems (Coles, 1993; Frank et al., 2001; Lester, LaGasse, & Seifer, 1998). Rather, the effects of PCE on school-aged children's language observed in this study after covariate control were relatively small and found only in specific subgroups of children. Although some have argued that subtle effects may have significant costs at a population level (Lester et al., 1998), it is unlikely that these differences would be clinically important for an individual child. When a child with PCE presents with language delays, clinicians should not assume that PCE alone is a sufficient explanation for the language problem but should initiate standard diagnostic and treatment protocols (including

audiological assessments) and address potentially modifiable environmental factors. From a policy perspective, broader interventions (Claussen et al., 2004) such as increasing children's participation in preschool educational programs and decreasing violence exposure may have positive effects on impoverished children's language development, regardless of their PCE status.

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Table I

Maternal and Caregiver Characteristics by Level of Prenatal Cocaine Exposure ($N = 160$)

	Level of prenatal cocaine exposure			Bivariate ^a <i>p</i> -value
	Unexposed (<i>n</i> = 75) % or <i>M</i> (<i>SD</i>) ^b	Lighter exposed (<i>n</i> = 57) % or <i>M</i> (<i>SD</i>) ^b	Heavier exposed (<i>n</i> = 28) % or <i>M</i> (<i>SD</i>) ^b	
<i>Birth mother</i>				
African American/Caribbean (%)	90.7%	84.2%	92.9%	0.38
Primiparous (%)	44%	26.3%	35.7%	0.11
U.S.-born (%)	74.7%	94.7%	100%	0.00
Age (years) at child's birth	25.3 (5.5)	27.8 (4.6)	27.6 (3.9)	0.01
Education (years) at child's birth	11.6 (1.4)	11.6 (1.4)	11.5 (1.1)	0.86
<i>Prenatal substance use</i>				
Average daily number of prenatal cigarettes	2.8 (7.4)	5.7 (6.4)	11.2 (13.4)	0.00
Average daily volume of alcohol during last 30 days of pregnancy	0.002 (0.1)	0.29 (1.1)	1.05 (3.0)	0.01
Prenatal marijuana use (any) (%)	9.3%	31.6%	35.7%	0.00
<i>Caregiver at 6- and 9.5-year visits</i>				
Verbal ability standard score ^c	84.5 (13.8)	84.6 (15.5)	91.1 (14.6)	0.10
<i>Education (years)</i>				
At 6-year visit	11.7 (1.4)	11.7 (2.3)	12.6 (2.8)	0.09
At 9.5-year visit	12.1 (1.9)	12.0 (1.7)	12.9 (2.9)	0.14
<i>Married or living with partner (%)</i>				
At 6-year visit	43.5%	23.1%	7.4%	0.06
At 9.5-year visit	39.7%	36.9%	20.0%	0.21
<i>Employed (%)</i>				
At 6-year visit	28.9%	23.1%	37.05	0.42
At 9.5-year visit	58.7%	39.1%	32.0%	0.03
<i>Received public assistance^d (%)</i>				
At 6-year visit	88.4%	75.0%	92.6%	0.06
At 9.5-year visit	22.7%	26.3%	25.0%	0.87
<i>Number of children in household</i>				
At 6-year visit	2.7 (1.3)	2.9 (1.6)	3.3 (1.8)	0.23
At 9.5-year visit	2.7 (1.3)	3.0 (2.0)	3.3 (1.8)	0.29
<i>Number of adults in household</i>				
At 6-year visit	1.8 (0.9)	1.8 (0.9)	1.9 (0.9)	0.97
At 9.5-year visit	1.7 (0.7)	1.7 (0.7)	1.8 (0.8)	0.84
<i>Child's caregiver at 6 years (%)</i>				
Birth mother	97.4%	59.7%	60.7%	
Kinship caregiver	0.0%	26.3%	25.0%	
Nonkin foster caregiver	2.6%	14.0%	14.3%	0.00
<i>Child's caregiver at 9.5 years (%)</i>				
Birth mother	97.4%	64.3%	50.0%	
Kinship caregiver	1.3%	23.2%	35.7%	
Nonkin foster caregiver	1.3%	12.5%	14.3%	0.00
<i>Caregivers' self-reported substance use</i>				
<i>Average daily number of cigarettes</i>				
At 6-year visit	0.29 (0.5)	0.44 (0.5)	0.56 (0.5)	0.04
At 9.5-year visit	0.32 (0.5)	0.47 (0.5)	0.36 (0.5)	0.23
<i>Any alcohol use (past 30 days) (%)</i>				
At 6-year visit	46.4%	40.4%	37.0%	0.65
At 9.5-year visit	38.1%	39.1%	52.0%	0.47
<i>Any marijuana use (past 30 days) (%)</i>				
At 6-year visit	7.3%	9.6%	11.1%	0.81
At 9.5-year visit	7.9%	2.2%	12.0%	0.25
<i>Any cocaine use (past 30 days) (%)</i>				
At 6-year visit	0.0%	3.9%	0.0%	0.15
At 9.5-year visit	0.0%	0.0%	0.0%	
<i>Psychosocial adaptation</i>				
<i>Psychological distress (BSI GSI)^e</i>				
At 6-year visit	0.31 (0.4)	0.28 (0.5)	0.35 (0.5)	0.85
At 9.5-year visit	0.36 (0.5)	0.22 (0.3)	0.18 (0.2)	0.07
<i>Total functional social support^f</i>				
At 6-year visit	77.7 (44.0)	84.8 (51.4)	87.7 (52.9)	0.59
At 9.5-year visit	52.9 (29.9)	66.9 (43.1)	59.8 (37.6)	0.14

Sample includes 160 subjects with at least one language assessment at the 6 or 9.5-year visits.

^aChi square or one-way ANOVA, as appropriate.^b*M* (*SD*), arithmetic mean (standard deviation).

^c Kaufman Brief Intelligence Test (K-BIT) verbal score or Peabody Picture Vocabulary Test (PPVT) score (population mean = 100 ± 15).

^d Any receipt of food stamps, Aid to Families with Dependent Children (AFDC), or Transitional Assistance to Needy Families (TANF).

^e BSI, Brief Symptom Inventory; GSI, Global Severity Index.

^f Norbeck Social Support Questionnaire.

Table II

Children's Characteristics by Level of Prenatal Cocaine Exposure ($N = 160$)

	Level of prenatal cocaine exposure			Bivariate p -value ^a
	Unexposed ($n = 75$) % or M (SD) ^b	Lighter exposure ($n = 57$) % or M (SD) ^b	Heavier exposure ($n = 28$) % or M (SD) ^b	
Male gender (%)	54.7%	50.9%	50.0%	0.87
Birthweight (z -score ^c)	-0.06 (1.0)	-0.68 (0.74)	-0.95 (0.72)	0.00
Maximum blood lead level (micrograms per deciliter) through 4 years of age	9.07 (4.9)	9.06 (4.1)	11.18 (8.2)	0.32
Otitis-prone (%) ^d	32.4%	22.2%	13.0%	0.14
Age (years)				
At 6-year visit	6.12 (0.2)	6.16 (0.3)	6.12 (0.2)	0.65
At 9.5-year visit	9.83 (0.6)	9.77 (0.3)	9.75 (0.4)	0.69
General intelligence (WPPSI-R IQ ^e) at age four				
Full Scale IQ	82.5 (11.1)	81.1 (12.7)	86.3 (8.3)	0.32
Verbal IQ	83.5 (12.5)	82.6 (11.9)	85.5 (9.7)	0.63
Performance IQ	84.5 (11.3)	83.4 (13.7)	89.6 (7.8)	0.09
Low WPPSI-R IQ (<70) (%)				
Low Full Scale IQ	12.7%	17.7%	0.0%	0.07 ^f
Low Verbal IQ	18.1%	16.7%	8.3%	0.52
Low Performance IQ	9.7%	4.7%	0.0%	0.19
Receipt of early intervention services (birth to two years) (%)	19.4%	22.2%	37.5%	0.19
Preschool experience (e.g. Headstart) (%)	20.8%	24.1%	12.5%	0.51
Special education services or grade retention (%)				
At 6-year visit	8.8%	7.8%	3.9%	0.84 ^f
At 9.5-year visit	38.1%	37.8%	28.0%	0.65 ^f
Child has contact with father (%)				
At 6-year visit	68.1%	38.5%	44.4%	0.003
At 9.5-year visit	50.8%	52.2%	60.0%	0.73
Exposed to violence or victimized (caregiver or child) (%)				
At 6-year visit	55.1%	40.0%	66.7%	0.07
At 9.5-year visit	41.9%	30.4%	56.0%	0.11
In a homeless shelter (%)				
At 6-year visit	2.9%	5.8%	3.7%	0.86 ^f
At 9.5-year visit	4.8%	0.0%	0.0%	0.29 ^f

Sample includes 160 subjects with at least one language assessment at 6 or 9.5 years.

^a Chi square or one-way analysis of variance (ANOVA), as appropriate.

^b M (SD), arithmetic mean (standard deviation).

^c Adjusted for gestational age and gender.

^d Three or more otitis events in the child's first 24 months of life.

^e WPPSI-R, Wechsler Preschool and Primary Scales of Intelligence-Revised.

^f Fisher's exact test.

Table III
Bivariate Comparisons of Children's Language Scores at 6 and 9.5 Years by Prenatal Cocaine Exposure Status

Language standard scores	Prenatal cocaine exposure		F ratio ^b	p-value	Effect size ^e
	Unexposed M (SD) ^d	Exposed M (SD)			
6 years	n = 73	n = 84			
Receptive language ^d	94.1 (15.1)	90.8 (12.2)	2.28	0.13	-0.24
Expressive language ^d	92.6 (18.3)	91.1 (12.5)	0.39	0.53	-0.09
Total language ^d	92.4 (17.4)	90.5 (11.7)	0.68	0.41	-0.13
9.5 years	n = 64	n = 73			
Receptive language ^d	87.9 (18.0)	89.1 (16.4)	0.16	0.68	0.07
Expressive language ^d	90.3 (16.7)	89.7 (15.9)	0.04	0.84	-0.04
Total language ^d	88.3 (17.1)	88.4 (16.0)	0.00	0.96	0.01
Low language score (<70)	N (%)	N (%)	χ^2	p-value	OR (95% CI) ^e
6 years	n = 73	n = 84			
Low receptive language (%)	2 (2.7%)	3 (3.6%)	0.77	0.77	1.30 (0.22-7.59)
Low expressive language (%)	7 (9.5%)	3 (3.6%)	2.37	0.19 ^f	0.37 (0.10-1.39)
Low total language (%)	8 (10.9%)	2 (2.4%)	4.82	0.10 ^f	0.22 (0.05-1.00)
9.5 years	n = 64	n = 73			
Low receptive language (%)	9 (14.1%)	12 (16.4%)	0.15	0.70	1.16 (0.52-2.59)
Low expressive language (%)	7 (10.9%)	10 (13.7%)	0.24	0.63	1.24 (0.50-3.10)
Low total language (%)	6 (9.4%)	9 (12.3%)	0.31	0.79 ^f	1.30 (0.49-3.49)

Language variables were derived from the Test of Language Development: Primary-third edition (TOLD:P-3) at the 6-year visit (n = 157) and the Clinical Evaluation of Language Fundamentals—Revised (CELF-R) at the 9.5-year visit (n = 134).

^a M (SD), arithmetic mean (standard deviation).

^b One-way analysis of variance (ANOVA), degrees of freedom = 1, 155 at 6 years and 1, 133 at 9.5 years.

^c Cohen's d. Negative d indicates lower mean in the cocaine-exposed group. An absolute value for d of 0.2, 0.5, or 0.8 indicates small, medium, and large effects, respectively.

^d Standard score (population mean = 100, standard deviation = 15).

^e OR, odds ratio; CI, confidence interval.

^f Fisher's exact test.

Table IV
 Estimated Interaction Effects of Prenatal Cocaine Exposure (PCE) and Child Variables on Receptive, Expressive, and Total Language Scores, Adjusting for Child Age at Test and Other Covariates

Language variable ^a	Interaction effect	Adjusted mean (SE) ^b	Estimated difference ^c	95% CI ^d	p-value
Receptive language	PCE by child age	6 years Unexposed	96.55 (1.96)		
		Exposed	90.41 (1.43)	-6.14	-10.6, -1.68
	9.5 years	Unexposed	90.74 (1.87)		
		Exposed	89.66 (1.46)	-1.08	-5.07, 2.90
Expressive language	PCE by child gender	Female	102.62 (3.6)		
		Unexposed	93.34 (3.4)	-9.28	-15.15, -3.42
	Male	Unexposed	94.97 (4.0)		
		Exposed	95.34 (2.9)	0.37	-6.77, 7.51
	PCE by birthweight (z-score) ^e	Unexposed	98.47 (4.1)		
		Exposed	96.71 (4.0)	-1.76	-7.04, 3.52
Total language	PCE by child gender	Female	101.43 (4.3)		
		Unexposed	92.50 (4.1)	-8.93	-15.43, -2.42
	Male	Unexposed	101.46 (3.4)		
		Exposed	93.62 (3.4)	-7.84	-13.19, -2.49
	50th percentile ^f (z = 0.00)	Unexposed	94.77 (4.1)		
		Exposed	95.48 (2.9)	0.71	-5.95, 7.38
10th percentile ^f (z = -1.28)	Unexposed	98.47 (4.1)			
	Exposed	96.71 (4.0)	-1.76	-7.04, 3.52	0.51

Values from the multivariate general linear model/generalized estimating equations (GLM/GEE) model for each language variable were adjusted for prenatal cocaine exposure, child age at test, and all other covariates. The specific covariates included in each model and p values for significant covariate main effects are presented in the Results section.

^a Standard scores (population mean = 100, standard deviation = 15).

^b SE, standard error. The adjusted means and standard errors for the interaction effects for each language variable were computed from the estimated model parameters, adjusting for child age and the covariates included in that model.

^c Negative values indicate a lower mean in the cocaine-exposed group.

^d CI, confidence interval.

^e Adjusted for gestational age and gender.

^f The 50th and 10th percentile cutoffs for birthweight z-scores reflect population values (adjusted for gestational age and gender) derived from published norms tables (National Center for Health Statistics, 1993).