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Externalizing behavior and substance use related problems at 15 years in prenatally cocaine exposed adolescents

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A B S T R A C T

The effect of prenatal cocaine exposure (PCE) on externalizing behavior and substance use related problems at 15 years of age was examined. Participants consisted of 358 adolescents (183 PCE, 175 non-cocaine exposed (NCE)), primarily African–American and of low socioeconomic status, prospectively enrolled in a longitudinal study from birth. Regression analyses indicated that the amount of PCE was associated with higher externalizing behavioral problems ($\beta = .15$, $p = .02$). Adolescents with PCE were also 2.8 times (95% CI = 1.38–5.56) more likely to have substance use related problems than their NCE counterparts. No differences between PCE adolescents in non-kinship adoptive/foster care ($n = 44$) and PCE adolescents in maternal/relative care ($n = 139$) were found in externalizing behavior or in the likelihood of substance use related problems. Findings demonstrate teratologic effects of PCE persisting into adolescence. PCE is a reliable marker for the potential development of problem behaviors in adolescence, including substance use related problems.

Maternal substance use during pregnancy continues to be a serious public health problem, with approximately 200,000 infants exposed to illicit drugs in utero each year in the United States (SAMHSA, 2012). Prenatal drug exposure during critical windows of embryonic and fetal development may alter brain development due to teratogenic, epigenetic, or cytotoxic effects. Emerging evidence indicates that prenatal cocaine exposure (PCE) disrupts the monoaminergic neurotransmitter system (dopamine, norepinephrine, serotonin) in the prefrontal cortex, a brain region responsible for emotional and behavioral arousal and regulation, attention, and stress response (Mayes, 2002; Thompson, Levitt, & Stanwood, 2009). Prenatal disruptions in the developmental programming of an infant's behavioral regulatory system due to PCE may have lasting effects on behavioral regulation, manifested differently across development, including greater externalizing behavior problems in childhood and/or early substance use in adolescence (Minnes, Lang, & Singer, 2011). As the prefrontal cortex and its

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associated networks are still developing in adolescence, the extent of impairment associated with PCE warrants continued evaluation as children with PCE mature.

A review focused on the preschool years (Dixon, Kurtz, & Chin, 2008) provided conflicting evidence of PCE effects on behavior problems, probably reflecting methodological differences among studies in determination of exposure status, operationalization of outcome variables (direct observation vs. parent rating; broad- vs. narrow-band scores), sample composition, confounders controlled for, and inter-individual differences in vulnerability to cocaine effects. However, the effects of PCE on behavioral regulation at early school age and during preadolescence converge with few exceptions despite methodological variability (Ackerman, Riggins, & Black, 2010). In a study of 244 7 year-olds, PCE during the third trimester was related to both caregiver and teacher reported externalizing behavior problems (Richardson, Goldschmidt, Leech, & Willford, 2011). At the same age (7), Accornero and colleagues found no evidence linking PCE and behavior problems via parent report (Accornero, Anthony, Morrow, Xue, & Bandstra, 2006), but increased behavioral problems among PCE children were noted when behavior was rated by examiners blinded to exposure status (Accornero et al., 2011). Our previous studies also indicated PCE effects. At 6 years of age, associations between PCE and symptoms of oppositional defiant disorder and attention-deficit/hyperactivity disorder (ADHD) were reported using child self-report, although the same study found no differences for caregiver reported problems (Linares et al., 2006). At 9 years, PCE was related to greater odds of aggressive behavior ratings using caregiver report. In addition, girls with PCE were more likely to be rated by their caregivers as having clinically significant delinquent behavior than NCE girls, whereas no differences were found for boys (McLaughlin et al., 2011). Longitudinal studies also lend support for PCE effects on externalizing behavior problems (Bada et al., 2007, 2011) prior to adolescence. Our longitudinal analyses of caregiver reported, clinically elevated, behavioral problems at 4, 6, 9, and 10 years of age indicated PCE to be associated with higher rates of delinquent behaviors among girls (Minnes et al., 2010).

Findings regarding PCE effects on behavioral adjustment and early substance use during adolescence are just beginning to emerge. One recent longitudinal study reported that children with cocaine/poly-drug exposure were rated as having higher levels of caregiver-reported externalizing behaviors through age 15 years than those with no drug exposure (Bada et al., 2012). However, this study did not examine PCE specific effects.

Three studies assessed the effects of PCE on early substance use, producing mixed findings. Increased risk of early substance use (alcohol, tobacco & marijuana) initiation by age 16 (Frank et al., 2011) and cocaine use at age 14 (Delaney-Black et al., 2011) were reported for PCE adolescents, whereas another study (Warner, Behnke, Eyler, & Szabo, 2011) found no relationship between PCE and early adolescent (12.5 years) experimentation with cocaine. Our data also indicates adolescents with PCE use more alcohol, tobacco, and marijuana than their NCE counterparts by 15 years of age (Minnes et al., 2014).

Multiple factors can affect behavioral outcomes of adolescents with PCE including prenatal exposure to other drugs/alcohol (Singer, Arendt, Minnes, Farkas, & Salvator, 2000), elevated blood lead levels (Min et al., 2009), and environmental conditions related to maternal drug use. Women who use cocaine during pregnancy tend to use other substances, including alcohol, cigarettes, and marijuana, all of which have been linked to externalizing behavior problems (Goldschmidt, Day, & Richardson, 2000; Maughan, Taylor, Caspi, & Moffitt, 2004; Sood et al., 2001) and early adolescent substance use (Baer, Sampson, Barr, Connor, & Streissguth, 2003; Cornelius, Leech, Goldschmidt, & Day, 2000; Day, Goldschmidt, & Thomas, 2006; Goldschmidt, Cornelius, & Day, 2012; Monshouwer et al., 2011). Between 12.5% and 35% of high risk poly-drug exposed children had elevated blood lead levels ($\geq$10 μg/dL) during preschool assessment (Bandstra et al., 2002; Lumeng, Cabral, Gannon, Heeren, & Frank, 2007; Nelson, Lerner, Needlman, Salvator, & Singer, 2004), in contrast to the general population rate of 8.65% for African American children and 2.02% for Caucasian children (Meyer et al., 2003). Elevated lead levels may further predispose PCE children to delinquent behavior (Dietrich, Ris, Succop, Berger, & Bornschein, 2001; Needleman, Riess, Tobin, Biesecker, & Greenhouse, 1996) and tobacco use (Lane et al., 2008). Environmental factors associated with prenatal drug use, such as poor quality of the home environment, caregiver ongoing substance use and psychological distress, violence exposure (Bada et al., 2007, 2011; Frank et al., 2011), non-kinship adoptive/foster care placement (Linares et al., 2006), negative attachment to caregiver (Warner et al., 2011) and low levels of parental monitoring (Bohnert, Anthony, & Breslau, 2012; Laird, Criss, Pettit, Dodge, & Bates, 2008) may heighten the drug exposed child's vulnerability to maladaptive behavioral development and obscure the long-term effects of PCE. In contrast, positive environmental factors may be protective or compensate for earlier biologic risk factors (Bada et al., 2012; Singer, 2004, 2008).

The purpose of the present study is to extend our previous studies of the effects of PCE into adolescence controlling for confounding factors of prenatal drug exposures, lead, and environmental covariates. Earlier behavioral problems may resolve or may become more pronounced in response to greater developmental demands of adolescence (puberty, academic performance/success, changing relationships with parents and peers). However, there are few prospective studies on adolescents, and this study represents one of the first prospective studies examining PCE effects during adolescence. An advantage of the current cohort is that a significant proportion of PCE children were placed in foster/adoptive care with lower lead levels and better home environments (Singer et al., 2008), allowing us to more specifically assess effects of PCE. We examined PCE effects on externalizing behavior problems in general as well as specific substance use related problems. Adolescents with PCE were hypothesized to report more externalizing behaviors and substance use related problems compared to adolescents who were non-cocaine exposed (NCE). Since our previous findings and those of others (Sood et al., 2005) have implicated gender as an important individual difference factor, we also explored whether the PCE effect on behavioral outcomes was moderated by gender.

Methods

Sample

This study included 358 (183 PCE, 175 NCE) 15 year old adolescents recruited at birth from a metropolitan teaching hospital and their birth mothers or current caregivers (Singer et al., 2002). Pregnant women who lacked prenatal care, exhibited behavior suggesting intoxication, had a history of involvement with the Department of Human Services, or self-admitted drug use, were considered to be high risk for drug use and given drug toxicology screenings at infant birth. Maternal and infant urine samples were obtained shortly before or after infant birth by medical staff and analyzed to detect the presence of cocaine metabolites, cannabinoids, opiates, phencyclidine, and amphetamines, using the Syva Emit method (Syva Co, Palo Alto, CA). Detection of drug use was confirmed with follow-up gas chromatography. In addition to urine analysis, infant meconium was collected and analyzed for cocaine and other drug metabolites at birth, including benzoylecgonine, meta-hydoxybenzoylecgonine, cocaethylene, cannabinoids, opiates, phencyclidine, amphetamines, and benzodiazepines. Women with a psychiatric history (major depression, bipolar disorder, or schizophrenia) (16), low intellectual functioning (1), HIV-positive status (5), or chronic medical illness (4) were excluded, as were infants with Down Syndrome (2), Fetal Alcohol Syndrome (1), or medical illness (3). A total of 415 newborns and their birth mothers were enrolled at birth, of which 218 infants were identified as cocaine exposed based on positive screens of maternal and infant urine, infant meconium, or maternal self-report to hospital or research staff (See Arendt, Singer, Minnes, & Salvator, 1999 for a complete description of drug use assessment).

Since birth, 12 enrolled children died (9 PCE, 3 NCE). Causes of death for the PCE children included sudden infant death syndrome (SIDS) (4), cardiopulmonary arrest (1), pneumonia (1), accidental asphyxia (1), respiratory distress syndrome (1), and unknown illness (1). For the NCE children, causes of death were SIDS (2) and respiratory distress syndrome (1). At 15 years of age, 358 children, representing 89% of the living participants in the original study, completed self-assessment. Of the 45 adolescents not seen, the 26 PCE children were more likely to have birth mothers with lower scores on the Wechsler Adult Intelligence Scale-Revised (WAIS-R) Picture Completion subtest (used as a screening measure of nonverbal intelligence) compared to the study participants, and the 19 NCE children not seen were more likely to be White and exposed to higher prenatal tobacco than the participants.

Procedure

Adolescents and their caregivers were seen at the developmental research laboratory for approximately 5 hours at each follow-up visit. Data in the present study were taken from interviews conducted when the children were ages 2 and 4 (blood lead), 10 (caregiver reported externalizing behavior), 12 (parental attachment, parental monitoring, violence exposure) and 15 years (externalizing behavior and substance use related problems). All participants were given a monetary stipend for participation, along with lunch and assistance with transportation costs if needed. This study was approved by the Institutional Review Board of the participating hospitals. Parental written informed consent and child assent were obtained. A Certificate of Confidentiality (DA-98-91), exempting the study from legislative, judicial, or administrative attempts to obtain confidential information, was obtained from the Department of Health and Human Services.

Measures

Prenatal cocaine and other substance exposures

At the newborn visit birth mothers were asked to recall frequency and amount of drug use for the month prior to and for each trimester of pregnancy. The number of tobacco cigarettes and marijuana joints smoked, and the number of drinks of beer, wine, or hard liquor per week was computed, with each drink equivalent to 0.5 oz. of absolute alcohol. For cocaine, the number of "rocks" consumed and the amount of money spent per day were also noted, in addition to the dichotomous cocaine status (PCE, NCE) variable. Frequency of use was recorded for each drug on a Likert-type scale ranging from 0 (not at all) to 7 (daily use) and converted to reflect the average number of days per week a drug was used, except for cigarettes, which was collected as the number smoked per day. Frequency was multiplied by the amount used per day to compute an average use score for the month prior to pregnancy and for each trimester. These scores were then averaged to obtain a total average score. The drug assessment was updated with the child's current caregiver at each follow-up visit to obtain an assessment of recent (prior 30 day period) postnatal, caregiver drug use. The continuous drug variables were used in analyses.

Externalizing behavior and substance use related problems

Adolescent externalizing behavior was assessed at age 15 using the Youth Self-Report (YSR; Achenbach & Rescorla, 2001), a 105-item child self-rating of his or her own behavior designed to assess emotional, behavioral, and social problems in the last 6 months. Items are coded from *0 (not true)* to *2 (very often or often true)* and written at the 5th grade reading level. Resultant *T*-scores were standardized for gender and age with higher scores indicating more problem behaviors. For this investigation, *T*-scores of externalizing behaviors (i.e., aggression and rule-breaking behavior, including alcohol, tobacco, and drug use) were used; with internal consistency reliability (α) = .90 for this administration. *T*-scores $\geq$ 60 indicate ratings at or above the

borderline/clinical cut-off, and scores below this level are considered nonclinical in nature. At age 10, externalizing behavior was assessed by caregiver-report using the Child Behavior Checklist (CBCL; $\alpha = .95$), a parallel form to the YSR.

Substance use related problems were measured at age 15 by the 17-item Substance Use and Abuse Scale from the Problem Oriented Screening Instrument for Teenagers (POSIT; Rahdert, 1991), which is designed to detect social and legal problems associated with alcohol and other drug use. The psychometric properties of the POSIT have been widely tested on youth in outpatient substance abuse treatment (McLaney, Boca, & Babor, 1994), arrested youth (Dembo et al., 1996), and youth attending a general adolescent clinic (Knight, Goodman, Pulerwitz, & DuRant, 2001; Shrier, Harris, Kurland, & Knight, 2003), yielding α ranging from .77 to .86 (Knight et al., 2001; McLaney et al., 1994) and 1-week test–retest reliability of .77 (Knight et al., 2001). Respondents reporting $\geq$1 problem(s) associated with substance use were coded 1 (yes) due to skewed distribution.

Child, maternal, and caregiver characteristics

Birth, demographic, and medical characteristics were extracted from hospital birth records including maternal age and marital status at birth, years of education of the biological mother, number of prenatal care visits, parity, child's race and gender, and infant head circumference. A Hollingshead score of IV or V (Hollingshead, 1957) was used as an indicator of low socioeconomic status. Maternal vocabulary was assessed at birth using the Peabody Picture Vocabulary Test-Revised (PPVT-R; Dunn & Dunn, 1981) and updated using its third edition (PPVT-III; Dunn, Dunn, Williams, Wang, & Booklets, 1997) at age 6 and later assessments. The PPVT-R/PPVT-III are highly correlated with various measures of verbal IQ with α ranging from .73 to .84 and test–retest reliabilities of .76–.79. The Block Design (BD) and Picture Completion (PC) subtests of the WAIS-R (Wechsler, 1981) were used to estimate maternal non-verbal intelligence at birth, as they correlate highest with Performance IQ (.81 and .75 respectively). Maternal psychological distress was assessed using the Brief Symptom Inventory (BSI; Derogatis, 1992), a 53-item self-report questionnaire assessing the experience of nine primary symptoms in the past seven days: somatic complaints, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Items were rated on a 5-point scale (*0 = not at all* to *4 = extremely*) with higher scores indicating greater distress. The BSI Global Severity Index (GSI; $\alpha = .95$), the average rating of all 53 items, was computed at birth and each follow-up visit. At each visit, the child's placement (with either biological mother/relative or foster/adoptive caregiver) and changes, if any, in placement, defined by a change in both primary caregiver and physical setting lasting greater than one month, were noted and the data on the current caregiver were updated to provide concurrent assessment of caregiver intelligence and psychological distress in addition to drug use. At the 15 year visit, the quality of the caregiving environment was assessed using the Home Observation of the Environment-Early Adolescent version (EA-HOME; Caldwell & Bradley, 2003), and adolescents' intelligence was assessed using the Wechsler Intelligence Scales for Children-Fourth Edition (WISC-IV; Wechsler, 2003).

Blood lead

At ages 2 and 4 years, all children participated in a separate study of lead exposure (Nelson et al., 2004). Venous blood samples could not be obtained from some children due to lack of parental consent, excessive stress related to the blood draw, child sickness, or time constraints. Valid hematologic measures were available for 143 two-year and 274 four-year old children. Measures were averaged for the 122 children seen at both assessment points, resulting in 298 valid assessments. A greater percentage of African–American and married women and a lower percentage of foster parents consented to blood collection.

Blood collection and analyses of lead were performed by the affiliate University Hospital Laboratory Services Foundation, accredited by the College of American Pathologists and in compliance with Clinical Laboratory Improvement Amendments regulations. The lab was enrolled in the Centers for Disease Control and Prevention (CDC) proficiency testing program for blood lead and was Occupational Safety and Health Administration approved for blood lead analysis. Approximately 5 ml of venous blood was drawn by syringe into a lead free container containing an anticoagulant. Blood lead concentration was determined by atomic absorption spectrophotometry using a graphite furnace and matrix modification to eliminate chemical interferences (Varian). Elevated blood lead values were defined as $\geq$10 mg/dL as recommended by the CDC for descriptive purposes. Continuous lead values were used in the statistical analyses.

Parental attachment, parental monitoring, and violence exposure

Parental attachment, monitoring, and violence exposure were all assessed at age 12 using the Assessment of Liability and EXposure to Substance use and Antisocial behavior (ALEXSA; Ridenour, 2003), an illustration-based, audio, computer-assisted self-interview to assess antisocial behavior, substance involvement and associated risk factors for children ages 9–12. The psychometric characteristics of ALEXSA subscales have been demonstrated with good to excellent test–retest reliability and construct validities (Ridenour, Clark, & Cottler, 2009), criterion validity (Ridenour, Meyer-Chilenski, & Reid, 2012), as well as its cross-cultural equivalence across different races/ethnicities, risk levels, and academic skills (Ridenour et al., 2011).

The ALEXSA parental attachment subscale is a 5-item questionnaire ($\alpha = .80$) designed to assess the youth's perceived strength of emotional bond with parents *(e.g.* "*How often does your parent listen to what you say?*" "*How often do you share your thoughts and feelings with your parent?*"). Children rated the frequency using a 4-point Likert scale (*0 = never* to *3 = all the time*) with higher scores indicating higher parental attachment.

Parental monitoring was measured by the ALEXSA with a 5-item questionnaire ($\alpha = .74$) designed to assess the youths' perceptions of whether their parent(s) usually are aware of the youths' activities and whereabouts with questions such as

"*Does your parent know none of the things you do in your free time (0), some of the things you do (1), most of the things you do (2), or all of the things you do in your free time (3)?*" "*Last week, did your parent know where you were going none of the times you left home (0), some of the times you left home (1), most of the time you left home (2), or all of the times you left home (3)?*" High scores indicate higher parental monitoring.

The violence exposure subscale on the ALEXSA is an 8-item questionnaire ($\alpha = .75$) assessing lifetime experiences of violence that have been inflicted directly on the respondent *(e.g.* "*How many times have you been beaten up?*" "*How many times have you been robbed or mugged?*") as well as violence that the respondent has witnessed *(e.g.* "How many times have you seen in person somebody get beat up (remember this does not count T.V. or movies)?" "How many times have you seen in person someone being robbed or mugged?"). Children rated the frequency of violence exposure using a 5-point Likert scale (*0 = 0 times* to *5 = 5 times or more*), with higher scores indicating greater exposure.

Statistical analyses

Data that were positively skewed were normalized using a log transformation (drug use, GSI on the BSI, violence exposure, and lead) prior to analyses. Means and standard deviations (SD) were reported by the variables' original distribution, with transformations used in analyses. Sample characteristics were examined by cocaine status using *t*-tests for continuous variables or Chi-square analyses for categorical variables. Zero-order Pearson correlations were estimated to examine relationships between study variables. The effects of PCE were evaluated using multiple regression on the YSR externalizing behavior scale and logistic regression on the POSIT substance use related problems.

In order to avoid multicollinearity and saturation of the model, covariates correlated with outcomes at $p \leq .20$ were entered into the regression model stepwise (i.e., using a series of steps) and were retained if, on entry, they were significant at $p < .10$ or caused substantial (>10%) change in the PCE coefficient (Mickey & Greenland, 1989). PCE was entered first followed by socio-demographic covariates (maternal age and education, parity, number of prenatal visits, maternal/caregiver's vocabulary ability, non-verbal reasoning, psychological distress, quality of home environment; adolescent age, sex, race), other drug exposure (prenatal tobacco, alcohol, and marijuana exposure), parenting (parental attachment and monitoring), and violence exposure variables. Due to the reduced sample size, blood lead level was entered last. If cocaine status was significant in the final model, average amount of PCE was examined. If results did not differ between a model with cocaine status (yes vs. no) and a model with amount of PCE, a model with amount of PCE was presented. Placement differences (PCE biologic/relative, PCE foster/adoptive care and NCE) were also evaluated using chi-square analyses, analyses of variance (ANOVA), or analyses of covariance (ANCOVA). Multicollinearity was examined using tolerance and variance inflation factor. Child gender was examined as a potential moderator of PCE effects.

Results

Sample characteristics

The birth mothers of adolescents with PCE had less prenatal care, were approximately 4 years older, slightly less educated, and primarily unmarried. They had lower vocabulary scores and reported more psychological distress than mothers of NCE adolescents (Table 1). Adolescents with PCE were exposed to more alcohol, marijuana, and tobacco prenatally, and had lower birth weight, length, and head circumference (Table 2). Caregiver and home environment characteristics at 15 years did not differ except that caregivers of the adolescents with PCE used more tobacco in the previous month. Adolescents with PCE had lower blood lead levels during the preschool years compared to NCE adolescents and were rated as having more externalizing problems by caregivers at age 10. Adolescents with PCE were less likely to be continuously cared for by their birth mothers, with 51% ($n = 94$) of adolescents with PCE, compared to 89% ($n = 156$) of their NCE counterparts, living with their birth parents, and 24% ($n = 44$) of adolescents with PCE, compared to 4.6% ($n = 8$) of their NCE counterparts, living in non-kinship adoptive/foster care ($\chi^2 = 24.32$, $p < .0001$) at the 15 year assessment. Adolescents with PCE reported a lower level of parental attachment at 12 years than their NCE counterparts, but no group differences were found in parental monitoring or violence exposure.

Adolescents with PCE reported more externalizing behavior problems ($M = 53.0$, SD = 10.47) than adolescents with NCE ($M = 50.6$, SD = 9.42; $p < .03$) and more substance use related problems (28% for PCE vs. 16% for NCE, $p = .008$) at 15 years. PCE adolescents were more likely to describe experiencing accidents, feelings of addiction, forgetfulness, and mood swings when using alcohol or drugs. However, no group difference was found in the proportion of adolescents scoring in the probable clinical range (*T*-scores ≥ 60) of externalizing behavioral problems (25% for PCE vs. 19% for NCE, $\chi^2 = 2.05$, $p = .15$). Externalizing behavior and substance use related problems were moderately correlated ($r = .29$, $p < .0001$). Zero-order Pearson correlations between key study variables are presented in Table 3.

Effects of PCE on YSR externalizing behavior at 15 years

Table 4 presents significant PCE effects on externalizing behavior at 15 years without (Model 1) and with (Model 2) controlling for earlier externalizing behavior. After adjusting for covariates (Model 1; $F = 6.84$, $p < .0001$), amount of PCE was associated with higher levels of externalizing behavioral problems ($\beta = .15$, $p = .02$). Birth mother's older age ($\beta = -0.12$,

Table 1
Maternal and current caregiver characteristics.

	PCE ($n = 183$)		NCE ($n = 175$)		p
	M	*SD*	*M*	*SD*	
Biological maternal					
Mother's age at birth	29.70	4.99	25.52	4.74	<.0001
Parity	3.50	1.83	2.77	1.87	.0002
Number of prenatal visits	5.18	4.59	8.69	4.85	<.0001
Education, years	11.55	1.65	11.93	1.38	.02
PPVT-R Standard Score	73.12	14.09	77.32	14.66	.007
WAIS-R Block Design Scaled Score	6.86	2.12	7.18	2.02	.15
WAIS-R Picture Completion Scaled Score	6.70	2.14	6.88	2.31	.44
BSI Global Severity Index	.82	.74	.50	.53	<.0001
Married, *n* (%)	14	7.65	28	16.00	.01
Low SES, *n* (%)	178	97.80	171	97.71	.96
African–American, *n* (%)	151	82.51	145	82.86	.93
Amount of substance use during pregnancy					
Tobacco, cigarettes per day	11.50	11.16	3.74	6.89	<.0001
Alcohol, dose per week	9.79	17.73	1.39	4.68	<.0001
Marijuana, dose per week	1.37	3.51	.62	3.58	<.0001
Cocaine, units per week	22.73	38.24	–	–	–
Caregiver at age 15 years					
Education, years	12.50	2.29	12.87	1.95	.10
PPVT-III Standard Score	79.95	14.89	78.73	15.08	.46
WAIS-R Block Design Scaled Score	7.10	2.13	7.23	1.92	.55
WAIS-R Picture Completion Scaled Score	7.53	2.52	7.08	2.30	.09
BSI Global Severity Index	.35	.42	.34	.47	.45
Amount of substance use in the past 30 days					
Tobacco, cigarettes per day	4.82	7.19	3.46	6.57	.01
Alcohol, dose per week	1.83	4.56	2.01	4.67	.49
Marijuana, dose per week	.54	5.48	.46	3.10	.61
HOME environment	47.59	6.90	48.71	6.16	.11

PPVT = Peabody Picture Vocabulary Test, PPVT-R (Revised) was used at birth; PPVT-III (Third edition) was used at age 6 and later years; WAIS-R = Wechsler Adult Intelligence Scale-Revised; BSI = Brief Symptom Inventory.

$p = .04$) and better HOME scores at 15 years ($\beta = -0.17$, $p = .001$) were related to fewer externalizing behavioral symptoms. Greater birth mother psychological distress ($\beta = .16$, $p = .005$) and violence exposure ($\beta = .23$, $p < .001$) was related to higher externalizing behavioral symptoms. Blood lead level was not associated with externalizing behaviors ($\beta = .04$, $p > .50$). Further adjustment of caregiver-reported earlier externalizing behavior didn't change the effect of PCE (Model 2; $F = 7.56$, $p < .0001$). No gender interaction was found.

Effects of PCE on POSIT substance use related problems at 15 years

Adolescents with PCE were at greater risk for substance use related problems than NCE adolescents (OR = 2.77, 95% CI = 1.38–5.56; Table 5). Adolescents with PCE were 2.8 times more likely to have substance use related problems than their NCE counterparts after adjusting for covariates. Higher parental monitoring decreased the likelihood of substance use related problems (OR = 0.63, 95% CI = 0.41–0.99) and better HOME scores were associated with a lower likelihood of substance use related problems (OR = 0.95, 95% CI = 0.91–0.99). Boys were 2.5 (95% CI = 1.37–4.71) times more likely to have substance use related problems than girls. Blood lead level was not associated with the likelihood of having substance use related problems (OR = 1.08, 95% CI = 0.58–1.98) nor was caregiver-reported externalizing behavior at age 10 (OR = 1.01, 95% CI = 0.98–1.03). No gender interaction was found.

Effects of adoptive/foster care status

PCE adolescents in non-kinship adoptive or foster care ($n = 44$) were exposed to cocaine more heavily ($M = 28.3$, SD = 43.6) than PCE adolescents in maternal or relative care ($n = 139$, $M = 21.97$, SD = 36.4) although the difference was not statistically significant ($F = 1.16$, $p = .28$). PCE adolescents in adoptive or foster care did not differ from those in maternal or relative care in maternal age at birth, birth mother's psychological distress (GSI), and prenatal alcohol exposure. However, their birth mothers had lower receptive vocabulary scores ($M = 68.4$, SD = 13.1) than mothers of PCE adolescents in maternal or relative care ($M = 74.6$, SD = 14.1) as well as mothers of NCE adolescents ($M = 77.3$, SD = 14.7; $F = 6.8$, $p = .001$). PCE adolescents in adoptive or foster care had a higher HOME score ($M = 50.9$, SD = 5.9) than PCE adolescents in maternal or relative care ($M = 46.6$, SD = 6.9; $F = 8.9$, $p < .0002$) and lower blood lead levels ($M = 5.8$, SD = 3.6) than NCE children ($M = 8.2$, SD = 4.6; $F = 4.5$, $p = .01$), a reason for overall lower blood lead levels observed among PCE adolescents. PCE adolescents currently residing in non-kinship adoptive or foster care had experienced 2.61 (SD = 2.54) placement changes on

Table 2
Adolescents characteristics.

	PCE ($n = 183$)		NCE ($n = 175$)		p
	M	*SD*	*M*	*SD*	
At birth					
Gestational age, weeks	37.73	2.86	38.46	2.90	.02
Hobel Neonatal Risk score	7.71	16.77	5.90	16.11	.30
Birth weight, g[a]	2700	655	3100	704	<.0001
Birth length, cm[a]	47.21	3.96	49.11	3.79	<.0001
Head circumference, cm[a]	32.26	2.17	33.48	2.40	<.0001
Prematurity (<37 wks gestational age), *n* (%)	55	30.05	33	18.86	.01
Low birth weight (<2500 g), *n* (%)	67	36.61	33	18.86	.0002
Very low birth weight (<1500 g), *n* (%)	12	6.56	7	4.00	.28
Small for gestational age, *n* (%)	25	13.81	4	2.30	<.0001
Microcephaly, *n* (%)	27	15.00	7	4.05	.0005
Male, *n* (%)	81	44.26	84	48.00	.48
African–American, *n* (%)	150	81.97	144	82.29	.94
Postnatal					
Blood lead level at 2 or/and 4 years[b]	7.06	4.16	8.16	4.64	.03
Elevated blood lead level (≥10 μg/dL[b]), *n* (%)	26	18.31	37	27.21	.08
Age at assessment, years	15.69	.27	15.67	.27	.50
Medicaid, *n* (%)	149	85.14	129	75.0	.02
Receiving free lunch at school, *n* (%)	145	83.33	143	84.62	.75
WISC-IV Full Scale IQ at 15	81.29	11.41	83.74	13.99	.07
Parental attachment[c]	2.10	.68	2.28	.61	.008
Parental monitoring[c]	2.43	.65	2.50	.58	.27
Violence exposure[c]	.63	.77	.59	.81	.54
Caregiver reported externalizing behavior at age 10	53.5	12.6	50.1	12.0	.009
Always in birth parents' care up to age 15, *n* (%)	60	32.8	132	75.4	<.0001
Current placement at 15, *n* (%)					<.0001
Birth parents' care	94	51.4	156	89.1	
Relative care	42	23.0	7	4.0	
Non-kinship adoptive care	38	20.8	5	2.9	
Others	9	4.9	7	4.0	
Non-kinship foster care	5	2.7	3	1.7	
Residential treatment[d]	3	1.6	2	1.1	
Group home	1	.5	2	1.1	

WISC-IV = Wechsler Intelligence Scales for Children-Fourth Edition.
[a] Adjusted for gestational age.
[b] Sub-sample of 142 PCE and 136 NCE.
[c] Assessed at 12 years.
[d] One adopted adolescent was in residential treatment.

average compared to PCE adolescents in maternal or relative care who had experienced 1.35 (SD = 1.54) placement changes and NCE adolescents who had experienced 0.65 (SD = 1.35) placement changes ($F = 27.8$, $p < .0001$). Of those 44 children with PCE in adoptive or foster care, 46% had only one placement change and 18% had two, indicating approximately two-thirds of them having been in somewhat stable living arrangements and one-third had experienced more than 2 placements. There

Table 3
Correlations between key variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Prenatal cocaine exposure (1 = yes)	–	.78	−.04	.40	.26	−.14	.49	−.09	−.14	−.06	.03	.14	.12	.14
2. Amount of prenatal cocaine exposure, units per week average		–	−.04	.29	.31	−.10	.49	−.02	−.11	−.06	−.05	.17	.16	.10
3. Child sex (1 = male)			–	−.07	−.06	.12	−.04	−.10	−.04	−.12	.08	.09	−.08	.18
4. Birth maternal age				–	.10	−.08	.28	.05	.01	−.04	.08	−.05	−.10	−.02
5. Birth maternal GSI at birth					–	−.11	.26	−.11	−.09	.00	−.07	.20	.19	.13
6. Maternal PPVT						–	−.11	.09	−.11	.04	−.07	.04	−.06	−.11
7. Prenatal alcohol dose per week average							–	−.03	−.12	−.07	.02	.14	.08	.06
8. HOME score								–	.10	.11	−.19	−.04	−.19	−.19
9. Parental attachment									–	.38	−.24	−.16	−.16	.00
10. Parental monitoring										–	−.29	−.12	−.15	−.16
11. Violence exposure											–	.18	.26	.14
12. Externalizing behavior (CBCL) at age 10												–	.28	.11
13. Externalizing behavior (YSR) at age 15													–	.29
14. Substance use related problems (POSIT) at age 15														–

Note. $p < .05$ when $r \geq |.11|$; $p < .01$ when $r \geq |.14|$.

Table 4
Effects of amount of prenatal cocaine exposure on adolescent self-reported externalizing behavior at 15 years.

	Model 1			Model 2		
	b (*se*)	*β*	*p*	*b* (*se*)	*β*	*p*
Prenatal cocaine exposure[a]	1.02 (.43)	.15	.02	.90 (.42)	.14	.03
Child sex, male	−1.96 (1.07)	−.10	.07	−2.21 (1.05)	−.11	.04
Birth maternal age	−.21 (.10)	−.12	.04	−.17 (.10)	−.10	.09
Biologic mother's GSI at birth	4.57 (1.65)	.16	.005	3.63 (1.64)	.13	.03
Prenatal alcohol exposure[b]	−.16 (.53)	−.02	.76	−.22 (.52)	−.03	.67
HOME score	−.27 (.09)	−.17	.001	−.29 (.08)	−.19	<.001
Parental attachment	−.49 (.90)	−.03	.59	−.33 (.88)	−.02	.71
Parental monitoring	−.82 (.95)	−.05	.39	−.70 (.93)	−.04	.45
Violence exposure	2.03 (.51)	.23	<.001	1.72 (.51)	.20	<.001
Externalizing behavior at age 10[c]				.15 (.04)	.19	<.001
R^2	.18			.21		

Note. Variables that were tested but not included in the final model because they were not significant at $p < .10$ or didn't cause substantial (>10%) change in the PCE coefficients are: birth mother education, parity, number of prenatal visits, maternal/caregiver vocabulary ability (PPVT-R), non-verbal reasoning (WAIS-R), adolescent age and race, prenatal tobacco and marijuana exposure, and blood lead level.

[a] Cocaine units per week.
[b] Average alcohol dose per week.
[c] Caregiver report (CBCL).

was no difference between the two PCE groups in parental attachment, parental monitoring, or violence exposure. After controlling for covariates, PCE adolescents in adoptive or foster care reported higher externalizing behavioral problems ($\beta = .17$, $p = .005$) and were more likely to have substance use related problems (OR = 2.98, 95% CI = 1.04–8.54) than NCE adolescents. There was no difference between the two PCE groups in externalizing behavior, as well as in the likelihood of substance use related problems.

Discussion

The present study demonstrated that PCE is associated with adolescent self-reported externalizing behavior and substance use related problems at 15 years of age. Our results are consistent with our previous findings at 6 years using child self-report (Linares et al., 2006) and 9 years using caregiver-report (McLaughlin et al., 2011). At 6 years, PCE children reported a higher average number of symptoms of oppositional defiant disorder and ADHD compared to NCE children. At 9 years, PCE was related to an increased likelihood of caregiver-reported aggressive behavior. The PCE-associated externalizing behavior problems, noted at 6 and 9 years, continued to be present at age 15 years. To our knowledge, this is one of the first prospective documentations of PCE-related effects on externalizing behaviors during adolescence. Our study is also in line with two prospective studies (Delaney-Black et al., 2011; Frank et al., 2011) indicating a greater risk of early substance use among PCE adolescents. PCE adolescents reported more substance related problems than their NCE counterparts, extending previous studies by demonstrating the extent of impairment in daily functioning for PCE adolescents via increased vulnerability to substance use. However, the gender by cocaine interaction on delinquent behavior, which had been shown at 9 years (McLaughlin et al., 2011) and from our longitudinal analyses of caregivers' ratings (Minnes et al., 2010), was not noted at age 15 years when self-report was employed. Differences in informants may explain the discrepancy, given the well-known, low cross-informant correlation that has been consistently demonstrated (Achenbach, 1991; De Los Reyes & Kazdin, 2005) with different correlates specific to the informant (Min, Singer, Minnes, Kim, & Short, 2013). Also, different developmental stages combined with confounders affecting gender differently may be responsible for the discrepancy. Compared to adolescent boys, adolescent girls are less exposed to violence (Bacchini, Miranda, & Affuso, 2011), monitored more by their parents

Table 5
Effects of prenatal cocaine exposure on adolescent self-reported substance use related problems at 15 years.

	b (*se*)	Odds Ratio (OR)	95% CI	*p*
Prenatal cocaine exposure	1.02 (.36)	2.77	1.38–5.56	.004
Child sex, male	.93 (.32)	2.54	1.37–4.71	.003
Maternal PPVT score	−.02 (.01)	.98	.96–1.00	.06
Prenatal alcohol exposure, average	−.12 (.14)	.89	.67–1.17	.39
Biologic mother's GSI at birth	.56 (.44)	1.75	.74–4.14	.21
HOME score	−.05 (.02)	.95	.91–.99	.04
Parental monitoring	−.46 (.23)	.63	.41–.99	.045
Pseudo R^2		.18		

Note. Variables that were tested but not included in the final model because they were not significant at $p < .10$ or didn't cause substantial (>10%) change in the PCE coefficients are: biological mother's age, education, parity, number of prenatal visits, maternal/caregiver non-verbal reasoning (WAIS-R), adolescent age and race, prenatal tobacco and marijuana exposure, parental attachment, violence exposure, blood lead level, and caregiver-reported externalizing behavior at age 10.

(Bacchini et al., 2011; Richards et al., 2004), and likely to be subjected to increased surveillance with the onset of puberty (Leadbeater, Kuperminc, Hertzog, & Blatt, 1999).

Consistent with our previous reports (Linares et al., 2006; McLaughlin et al., 2011; Minnes et al., 2010), PCE adolescents in adoptive or foster care reported higher externalizing behavioral problems than NCE adolescents, but no significant difference was found between PCE adolescents in maternal/relative care and NCE adolescents. These findings on behavioral outcomes in relation to adoptive/foster care placement are in contrast to our previous findings of cognitive and language outcomes during the preadolescent years, where better cognitive and language development was shown for PCE children in adoptive or foster care compared to PCE children in maternal or relative care (Lewis et al., 2011; Singer et al., 2004, 2008). Thus, a more positive postnatal caregiving environment provided by non-kinship adoptive/foster care appears not to have had the same protective impact on the behavioral domain as was shown on cognitive and language outcomes in PCE children. Less stability in the caregiving environment indicated by more placement changes in PCE adolescents in foster/adoptive care may affect behavioral adjustment by compromising children's ability to build stable relationships, which may again lead to another placement change (Aarons et al., 2010), generating a vicious cycle of disruption and worsening behavioral adjustment.

Other factors also contributed to externalizing behavior and substance use related problems at 15 years. Parental monitoring was associated with a lower likelihood of substance use related problems, while violence exposure was associated with increased externalizing behavior. The protective effects of parental monitoring is noteworthy, as they suggest prevention and/or intervention targets to reduce substance use related problems in adolescents with PCE.

Several limitations in our study should be noted. Children born prenatally exposed to cocaine are often placed outside of their birth mother's custody, and placement changes may negatively affect behavioral adjustment. Without a comparable number of NCE adolescents living in non-kinship adoptive/foster care, our study is limited in separating the effect of PCE from the effects of placement changes among PCE adolescents. Also, outcome variables of the present study relied on adolescents' self-report, which might be subject to social desirability bias, as well as adolescents' ability to accurately self-assess their behaviors. Although biological measures were used for detection of PCE in our study, maternal/caregivers' self-report was used for assessment of levels of prenatal and postnatal substance use, which may have resulted in underreporting of drug use and, thus, underestimation of the effects of PCE and other drugs.

Despite these limitations, this study has strengths including its prospective design assessing a large number of adolescents and their caregivers since birth with a high rate of retention (89%) at the 15 year follow-up. A comprehensive list of covariates and confounders, including other prenatal substance exposures and lead, were evaluated and controlled statistically when necessary. By incorporating non-kinship adoptive or foster care placement, which disproportionately occurred for adolescents with heavier PCE, our study attempted to tease out the effects of protective environmental factors related to placement among adolescents with PCE. Evaluation of covariates that are more pertinent to adolescence, such as adolescents' perceived parental attachment, monitoring, and violence exposure, enhanced our understanding of the dynamics of PCE, non-kinship adoptive or foster care, parenting, and adolescent behavioral adjustment.

The present study extends previous studies of PCE by providing evidence of the longitudinal effects of PCE persisting into adolescence. Controlling for confounding factors, PCE adolescents reported more externalizing behavioral problems and more substance use related problems. Our study suggests that PCE is a reliable marker for the potential development of problem behaviors in adolescence, including substance use related problems. Interventions focusing on strengthening parental monitoring and decreasing violence exposure may be promising in reducing behavioral problems among high risk prenatally cocaine/poly-drug exposed adolescents.

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