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Pathways to adolescent sexual risk behaviors: Effects of prenatal cocaine exposure

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ABSTRACT

Background: To assess the impact of prenatal cocaine exposure (PCE) on adolescent sexual risk behaviors. Externalizing behavior, teen substance use, and early sexual intercourse were examined as pathways mediating the effects of PCE on sexual risk behaviors.
Methods: Adolescents ($N = 364$; 185 PCE, 179 non-cocaine exposure (NCE); 205 girls, 159 boys), primarily African–American and of low socioeconomic status, were prospectively enrolled in a longitudinal study at birth. Risky sexual behaviors were assessed at ages 15 and 17. Externalizing behavior at 12 years was assessed with the Youth Self-Report. Substance use, via self-report and biologic assays, and early (before age 15) sexual intercourse were assessed at age 15. Path analyses with the weighted least squares estimator with mean and variance adjustments were performed.
Results: The final structural equation model-based path model, $\chi^2 = 31.97$ (df = 27), $p = .23$, CFI = .99, TLI = .99, RMSEA = .021, WRMR = .695, indicated a direct effect of PCE on sexual risk behavior ($\beta = .16$, $p = .02$). Although PCE was related to greater externalizing behavior ($\beta = .14$, $p = .009$), which in turn, predicted early sexual intercourse ($\beta = .16$, $p = .03$), leading to sexual risk behavior ($\beta = .44$, $p < .001$), bootstrapping indicated a non-significant indirect effect ($\beta = .01$, $p > .10$). Substance use was correlated with early sexual intercourse ($r = .60$, $p < .001$) and predicted sexual risk behavior by age 17 ($\beta = .31$, $p = .01$).
Conclusions: Prenatal cocaine exposure was related to more engagement in sexual risk behaviors, suggesting the importance of reducing substance use among pregnant women as a means of prevention of offspring substance use and sexual risk behavior.

1. Introduction

Sexual risk behaviors, including multiple sexual partners, infrequent condom and contraceptive use, and having sex under the influence of alcohol or drugs, contribute to unintended pregnancy and sexually transmitted infections (STIs) including HIV. Data from the 2013 Youth Risk Behavior Survey indicate that only 59% of sexually active high school (grades 9–12) students reported condom use during the last time they had sexual intercourse (Kann et al., 2014). Although sexually active teens and young adults (ages 15–24) represent only 25% of the sexually active population, they account for nearly half of new STI cases (Centers for Disease Control and Prevention (CDC), 2014) and 26% of all new HIV cases in the US (CDC, 2012). The 2003–2004 National Health and Nutrition Examination Survey (NHANES) indicated 38% of sexually experienced female adolescents aged 14–19 had laboratory evidence of STI (Forhan et al., 2009).

Prenatal cocaine exposure (PCE) may increase the vulnerability for adolescent sexual risk behavior (De Genna et al., 2014; Lambert et al., 2013; Min et al., 2015). Approximately 214,000 infants are exposed in utero to illicit drugs, including cocaine, each year in the United States (Substance Abuse and Mental Health Services Administration (SAMHSA), 2014); however, the effects of PCE on adolescent sexual behavior have not been well-established, with only three published studies from three prospective birth cohorts to date (De Genna et al., 2014; Lambert et al., 2013; Min et al., 2015). Although these studies indicated that, compared to non-cocaine exposed (NCE) adolescents, adolescents with PCE initiated sexual intercourse earlier (De Genna et al., 2014) and were more likely

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to have sexual intercourse (Min et al., 2015) or oral sex before age 15 (Lambert et al., 2013), they mainly focused on the age at first sexual intercourse. Only one study (Lambert et al., 2013) examined PCE effects on other sexual risk behaviors, reporting significant PCE effects on engaging in sex without a condom in boys only.

Multiple mechanisms may account for the link between PCE and sexual risk behavior. Maternal use of cocaine during pregnancy directly impacts the developing fetal brain by altering/disrupting the monoaminergic neurotransmitter system involving dopamine, serotonin, and norepinephrine in the prefrontal cortex (Kosofsky et al., 1994; McCarthy et al., 2014). Disruption in the prefrontal cortex has been implicated in problems of inhibitory control, attention, increased risk taking behaviors, and executive function (Thompson et al., 2009), all of which likely contribute to sexual risk behaviors (Goldenberg et al., 2013; Khurana et al., 2012). In addition, PCE may indirectly increase vulnerability to sexual risk behavior through biological and environmental confounders, including prenatal exposure to other substances such as alcohol (Larkby et al., 2011), tobacco (Maughan et al., 2004), and marijuana (Goldschmidt et al., 2000), ongoing parental substance abuse (Elkington et al., 2011) and psychological distress (Minnes et al., 2010), and elevated lead (≥10 μg/dL) levels (Lane et al., 2008; Min et al., 2009; Singer et al., 2008). Further, poor quality of the home environment (Singer et al., 2008) including poor attachment to caregiver (Warner et al., 2011) and inadequate parental monitoring (Min et al., 2014a,b), sexual victimization (De Genna et al., 2014), violence exposure (Frank et al., 2011), and adoptive/foster care placement (Singer et al., 2004) may obscure the effects of PCE. Prospective, longitudinal birth cohort studies demonstrated effects of PCE on externalizing behavior (Ackerman et al., 2010; Buckingham-Howes et al., 2013; Min et al., 2014a,b; Minnes et al., 2010) and substance use (Frank et al., 2011; Minnes et al., 2014; Richardson et al., 2013), well-known precursors to sexual risk behaviors (Ramrakha et al., 2007; Wu et al., 2010).

The present study examined the impact of PCE on sexual risk behaviors assessed at ages 15 and 17 using path analyses. We previously reported more externalizing behavior problems at age 12 (Min et al., 2014b) and greater alcohol, tobacco and marijuana use (Minnes et al., 2014) and substance related problems (Min et al., 2014a) at age 15 in adolescents with PCE. We also found that adolescents with PCE were more likely to engage in early (<age 15) sexual intercourse (Min et al., 2015). Thus, in the present study, we examined externalizing behavior, substance use, and early sexual intercourse as pathways mediating the effects of PCE on sexual risk behaviors. We also tested whether PCE had unique effects on sexual risk behavior over and above its indirect influences. We hypothesized that PCE would be related to externalizing behavior and that externalizing behavior would predict substance use and early sexual intercourse, leading to sexual risk behaviors. Since both substance use and early sexual intercourse were assessed at age 15, correlation between these two variables was included in the path model. A direct path from PCE to sexual risk behavior was also specified in the model to indicate other unmeasured mediators of PCE.

2. Method

2.1. Sample

This study included 364 (185 PCE, 179 NCE) adolescents recruited at birth (September 1994–June 1996) from an urban county hospital and their birth mothers or caregivers for a longitudinal investigation of the effects of PCE. Pregnant women who had a urine toxicology screening at delivery due to a lack of prenatal care, behavior suggesting intoxication, self-admitted substance use, or a history of involvement with the Department of Human Services, were eligible for the study. Women with a psychiatric history, low intellectual functioning indicated in medical chart review, HIV-positive status, or chronic medical illness were excluded, as were infants with Down syndrome, fetal alcohol syndrome, or congenital heart defects. A nurse recruiter approached 647 screened women immediately before or after infant birth; of these 647 women, 54 were excluded, 155 refused to participate, and 23 did not come to the enrollment visit.

Maternal and infant urine samples and infant meconium were obtained shortly before or after infant birth and analyzed for cocaine and other drug metabolites, including benzoylecgonine, meta-hydroxybenzoylecgonine, cocaethylene, cannabinoids, opiates, phencyclidine, amphetamines, and benzodiazepines. 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. Infants who were negative on all indicators of prenatal cocaine exposure were identified as NCE. Subjects and their caregivers were assessed by separate examiners who were blinded to exposure status at follow-up assessments at 6, 12, and 18 months and 2, 4, 6, 9–12, 15, and 17 years postpartum.

Since birth, 12 (9 PCE, 3 NCE) enrolled children died from sudden infant death syndrome (4 PCE, 2 NCE), cardiopulmonary arrest (1 PCE), pneumonia (1 PCE), accidental asphyxia (1 PCE), respiratory distress syndrome (1 PCE, 1 NCE), and unknown illness (1 PCE). The present study utilizes data from 364 adolescents who completed sexual behavior assessment at age 15 and/or 17 years, representing 90% retention of the 403 living participants in the original study. Among the 364 participating adolescents, 92.6% ($n = 337$) were assessed at both 15 and 17 years of age. Of the 39 adolescents not included in these analyses (19 drop-out, 18 lost contact, 2 low intellectual functioning (IQ < 50)), the 24 PCE adolescents did not differ from the 185 participating PCE adolescents. The 15 NCE adolescents not included in the study were more likely to be white, have birth mothers who were older, more likely to be married, and had more years of education compared to the 179 participating NCE adolescents. The Institutional Review Board of the participating hospital approved this study. All participants were given a monetary stipend, lunch, and transportation costs if needed. Parental written informed consent was obtained, with child assent beginning at age 9. A Certificate of Confidentiality (DA-09-146) was obtained from the U.S. Department of Health and Human Services to protect identifiable research information from forced disclosure.

2.2. Measures

2.2.1. Prenatal cocaine and other substance exposure. 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, as the majority of women (97%) in our study used the crack cocaine form, the number of "rocks" consumed and the amount of money spent per day were noted, which was converted to a standard "unit" of cocaine, referring to $20 worth of cocaine. No sociodemographic difference was found between women ($n = 11$) who used a non-crack cocaine form and 353 women who used crack cocaine. However, the 11 women used more marijuana, and less alcohol and cocaine compared to the 353 women who reported using crack cocaine. 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 average drug summary variables were used in path analyses.

2.2.2. Sexual risk behaviors. Risky sexual behaviors were assessed at ages 15 and 17 using items from the Youth Risk Behavior Surveillance System (YRBSS; CDC, 2009): (1) ≥2 sexual partners during the past 3 months, (2) drank alcohol or used drugs before sexual intercourse, (3) no condom use, (4) no method used to prevent pregnancy in the last time of sexual intercourse, and (5) ever been pregnant or made someone pregnant. These five variables were combined to form a composite sexual risk behavior variable. Respondents reporting ≥1 risky sexual behavior(s) at either the 15 or 17 year assessment were coded 1 (yes).

2.2.3. Confounders. Birth, demographic, and medical characteristics (e.g., maternal age and marital status at birth, years of education of the biological mother, child's race and gender, infant head circumference, etc.) were extracted from hospital birth records. Maternal/caregiver self-reported psychological distress was assessed using the Global Severity Index (α=.95), a summary scale of the Brief Symptom Inventory (BSI; Derogatis, 1992) at birth and each follow-up visit. The child's placement (with either biological mother/relative or adoptive/foster caregiver) was also noted at each visit, with updated assessment of the current caregiver's psychological distress if there had been a change in caregiver. Blood lead (μg/dL) was assessed for a subset of children at ages 2 and 4 years. Venous blood samples could not be obtained from some children due to lack of parental consent, excessive stress related to having blood draw, child sickness or logistical difficulties. Valid hematologic measures were available for 143 two-year and 274 four-year old children. If blood lead was measured at both assessments, then measures were averaged (n = 122). A greater percentage of African-American and married women and a lower percentage of foster parents consented to blood collection. Parental attachment (α=.80) and monitoring (α = .74), violence exposure (α=.75), and pubertal development (α = .82 for girls; α = .76 for boys) were all assessed at the 12 year visit using The Assessment of Liability and Exposure to Substance Use and Antisocial Behavior (ALEXSA; Ridenour et al., 2009) an illustration-based, audio, computer-assisted self-report of antisocial behavior, substance involvement and associated risk factors for children ages 9–12. The quality of the caregiving environment was also assessed at the 12 year visit using the Home Observation of the Environment-Early Adolescent version (EA-HOME; α = .83; Caldwell and Bradley, 2003). Adolescents' intelligence was assessed at age 15 using the Wechsler Intelligence Scales for Children-Fourth Edition (Wechsler, 2003). Sexual victimization was assessed (1 = yes; 0 = no) retrospectively at age 17 using the Juvenile Victimization Questionnaire (Hamby et al., 2004).

2.3.4. Mediators. Externalizing behavior (aggression and rule-breaking behavior) was assessed at age 12 using the Youth Self-Report (Achenbach and 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. *T*-scores were standardized for gender and age, with higher scores indicating more problem behaviors (α = .87). Adolescent's substance use was assessed at age 15 using self-report and biologic assays. Self-reported alcohol, tobacco, and marijuana use were assessed using the YRBSS. Research nurses from the university's NIH-funded Clinical Research Unit collected samples of participants' urine, hair, and/or bloodspots, which were sent to the United States Drug Testing Laboratory for analysis (see Minnes et al., 2014 for a complete description of drug use assessment). Respondents who were positive on either self-report or biologic assays for a particular drug were coded 1 (yes) for that drug. Seventy-eight percent (87/111) of adolescents who were positive on tobacco use were based on self-report only, with 4.5% (n = 5) and 17% (n = 19) based on biological samples and both measures respectively. For alcohol, 95% (129/136) of adolescents who were positive on alcohol use were based on self-report only, with 1.5% (n = 2) and 3.7% (n = 5) based on biological samples and both measures respectively. For marijuana, 71% (76/107) of adolescents who were positive on marijuana use were based on self-report only, with 3.7% (n = 4) and 25.2% (n = 27) based on biological samples and both measures respectively. Substance use was specified as a latent variable (α = .74) with three indicators (alcohol, tobacco, and marijuana) for path analyses. Early sexual intercourse, defined as sexual intercourse prior to age 15, was assessed at age 15 using the YRBSS.

2.3. Data analyses

Path analyses were conducted using Mplus version 7.11 to evaluate the direct and indirect effects of PCE as well as associations between observed and latent variables. Since the primary outcome variable was binary, the weighted least squares estimator with mean and variance adjustments (WLSMV) was used, which computes ordinary least squares parameter estimates for continuous outcomes and probit parameter estimates for categorical outcomes. Model fit was evaluated with the robust WLSMV chi-square, comparative fit index (CFI), Tucker-Lewis Index (TLI), root mean square error of approximation (RMSEA), and the weighted root mean square residual (WRMR). Values ≥ .95 for CFI and TLI, ≤ .06 for RMSEA (Hu and Bentler, 1998), and ≤ .09 for WRMR (Yu and Muthén, 2002) indicate a good fit. Missing data on endogenous variables were estimated as a function of the observed exogenous variables under the assumption of missing completely at random. Violence exposure, home environment quality, lead level, and sexual victimization were included in the model as covariates since they were correlated (p < .10) with the outcome. Sex was also included as a covariate since our previous study (Min et al., 2015) indicated greater likelihood of boys engaging in early sexual intercourse than girls. Other covariates including other prenatal substance (alcohol, tobacco, marijuana) exposure were not related to the endogenous variables and were not included in the model A bootstrap approach in which the standard error is computed based on 5000 bootstrap replicates was used to test for indirect effects (Preacher and Hayes, 2008). Competing nested models were compared using the derivatives difference test (Muthén and Muthén, 2012), which compares nested models under the WLSMV estimator.

3. Results

3.1. Sample characteristics

Table 1 presents characteristics of birth mothers, caregivers at age 12, and adolescents. The birth mothers of adolescents with PCE were older, less educated, had greater psychological distress, were less likely to be married, and reported greater use of tobacco, alcohol, and marijuana over their pregnancy than birth mothers of NCE adolescents. The average amounts of drug use generally declined over the course of pregnancy in both groups: 83% (n = 154) of cocaine using mothers reported 36 (SD = 62) units of crack cocaine per week in the month prior to pregnancy on average, compared to

Table 1
Sample characteristics.

	PCE (n = 185)		NCE (n = 179)		p
	n (%)	M (SD)	n (%)	M (SD)	
Biological mother					
Mother's age at birth		29.77 (5.01)		25.45 (4.72)	<.001
Education, years		11.56 (1.67)		11.92 (1.38)	.02
BSI Global Severity Index[a]		.83 (.75)		.51 (.54)	<.001
Married	15 (8.11)		28 (15.64)		.03
Low SES	180 (97.83)		175 (97.77)		.97
African–American	152 (82.16)		146 (81.56)		.88
Substance use during pregnancy[a,b]					
Tobacco, cigarettes per day	157 (84.86)	11.55 (11.08)	69 (38.55)	3.85 (7.13)	<.001
Alcohol, drinks per week	145 (78.38)	9.80 (17.64)	72 (40.22)	1.38 (4.64)	<.001
Marijuana, joints per week	77 (41.62)	1.35 (3.48)	16 (8.94)	.61 (3.55)	<.001
Cocaine, units per week	185 (100)	22.61 (38.05)	–	–	–
Caregiver at age 12					
Education, years		12.04 (2.39)		12.74 (1.89)	.003
BSI Global Severity Index		.35 (.45)		.36 (.49)	.95
Home environment		47.83 (6.86)		49.06 (6.28)	.07
Substance use in the past 30 days[a,b,c]					
Tobacco, cigarettes per day	86 (46.49)	5.30 (7.41)	64 (35.75)	3.83 (6.72)	.04
Alcohol, dose per week	53 (28.65)	1.45 (3.74)	57 (31.84)	1.75 (5.54)	.51
Marijuana, dose per week	8 (4.32)	.91 (7.18)	4 (2.23)	.10 (1.09)	.26
Adolescents					
Gestational age, weeks		37.82 (2.78)		38.47 (2.88)	.03
Hobel neonatal risk score		7.27 (15.70)		5.88 (15.95)	.40
Birth weight, grams[d]		2714 (645)		3104 (702)	<.001
Birth length, cm[d]		47.33 (3.89)		49.15 (3.76)	<.001
Head circumference, cm[d]		32.31 (2.11)		33.47 (2.40)	<.001
Blood lead level, μg/dL[a,e]		7.07 (4.14)		8.04 (4.66)	.06
Parental attachment[f]		2.10 (.68)		2.27 (.61)	.01
Parental monitoring[f]		2.42 (.65)		2.49 (.58)	.32
Violence exposure[a,f]		.63 (.77)		.58 (.80)	.47
Pubertal development[f]		1.27 (.57)		1.25 (.57)	.79
YSR Externalizing behavior[f]		50.99 (10.05)		47.79 (9.75)	.002
WISC-IV Full Scale IQ[g]		81.35(11.27)		83.80 (14.01)	.07
Male	74 (42.05)		85 (48.02)		.26
African–American	151 (81.62)		145 (81.01)		.88
Receiving medicaid[g]	152 (85.39)		129 (75.00)		.01
Receiving free lunch at school[g]	148 (83.62)		143 (84.62)		.80
Always in birth parents' care[g]	57 (30.81)		134 (74.86)		<.001
Placement at 15					<.001
Birth parents' care	95 (51.35)		160 (89.39)		
Relative care	37 (20.00)		6 (3.35)		
Non-kinship care	44 (23.78)		6 (3.35)		
Others	9 (4.86)		7 (3.91)		
Sexual victimization	36 (21.05)		34 (19.77)		.77
Substance use at age 15					
Tobacco	64 (35.36)		47 (27.17)		.10
Alcohol	72 (39.56)		64 (36.57)		.56
Marijuana	64 (35.16)		43 (24.57)		.03
Early (<age 15) sexual intercourse	69 (38.33)		49 (28.16)		.04

BSI = Brief Symptom Inventory; WISC-IV = Wechsler Intelligence Scales for Children-Fourth Edition. YSR = Youth Self Report.
[a] Data were normalized using a log transformation.
[b] p-value based on n (%).
[c] No caregivers reported cocaine use in the past 30 days.
[d] Adjusted for gestational age.
[e] Sub-sample of 145 PCE and 139 NCE.
[f] Assessed at age 12.
[g] Assessed at age 15.

74% (n = 136) of cocaine using mothers reported 16 (SD = 31) units of crack cocaine per week in the third trimester. No difference was found in caregiver characteristics at age 15, except that caregivers of the adolescents with PCE had less education and smoked more cigarettes in the past 30 days than the caregivers of NCE adolescents. Adolescents with PCE had a shorter gestational age, lower birth weight, length, and head circumference; reported a lower level of parental attachment and more externalizing behavior problems at age 12; and were less likely to be continuously cared for by their birth parents than the NCE adolescents. Although simple group comparisons indicated a PCE group difference only in marijuana use, multivariate analyses controlling for confounders indicated significant PCE effects on alcohol and tobacco, as well as on marijuana (Minnes et al., 2014). PCE adolescents were more likely to engage in sexual intercourse before age 15.

The prevalence of sexual risk behaviors is presented in Table 2. By age 17, 76% (n = 140) of adolescents with PCE and 68% (n = 121) of adolescents with NCE experienced sexual intercourse. Almost half (46%, n = 85) of PCE adolescents and 38% (n = 68) of NCE adolescents reported sexual risk behaviors, indicating 61% of PCE and

Table 2
Risky sexual behavior by cocaine status and age ($N = 364$).

	Total			15 year			17 year		
	PCE ($n = 185$)	NCE ($n = 179$)	p	PCE ($n = 180$)	NCE ($n = 174$)	p	PCE ($n = 172$)	NCE ($n = 175$)	p
Test age, M (SD)	–	–		15.69 (.27)	15.67 (.27)	.53	17.82 (.26)	17.79 (.26)	.37
Ever had sexual intercourse, n (%)	140 (75.68)	121 (67.60)	.09	88 (48.9)	69 (39.7)	.08	128 (74.4)	112 (64.4)	.04
Risky sexual behavior, n (%)	85 (46.0)	68 (38.0)	.12	24 (13.3)	28 (16.9)	.46	77 (44.8)	59 (33.7)	.035
≥2 sexual partners during the past 3 months	28 (15.14)	36 (20.11)	.21	12	16		25	26	
Drank alcohol or used drugs before sexual intercourse[a]	20 (14.18)	10 (8.33)	.14	7	4		13	7	
No condom use[a]	45 (31.91)	32 (26.89)	.38	12	12		37	27	
No method used to prevent pregnancy[a]	23 (12.50)	26 (14.53)	.57	6	11		17	17	
Ever been pregnant or made someone pregnant	30 (16.85)	25 (14.12)	.48	4	1		30	25	

[a] In the last time of sexual intercourse.

Table 3
Correlations among observed variables in a path model.

	1	2	3	4	5	6	7	8	9	10	11	12
1. Prenatal cocaine exposure[a]	–	−.03	−.04	−.04	.09	−.09	.13*	.001	.07	.07	.09	.13*
2. Gender, male		–	.08	−.08	.05	−.03	.06	.04	.02	.10*	.24***	.07
3. Violence exposure			–	−.07	.08	.13*	.42***	.06	.14*	.23***	.28***	.22***
4. Home score				–	.07	−.15*	−.09	−.02	−.04	−.12*	−.17**	−.13*
5. Sexual victimization					–	.003	.18***	.10	.27***	.15**	.17**	.20***
6. Blood lead level[b]						–	−.05	.07	.02	.10	.20**	.15*
7. Externalizing behavior							–	.09	.20***	.18***	.24***	.14**
Substance use												
8. Alcohol								–	.43***	.47***	.26***	.24***
9. Tobacco									–	.56***	.33***	.24***
10. Marijuana										–	.46***	.41***
11. Early sex											–	.46***
12. Sexual risk behavior												–
M	1.18	–	−.94	48.44	–	1.86	49.41	–	–	–	–	–
SD	.1.48	–	1.11	6.60	–	.57	10.02	–	–	–	–	–
%	–	46.70	–	–	20.41	–	–	38.10	31.36	29.97	33.33	42.03

[a] Cocaine units per week, log transformed.
[b] Sub-sample of 284.
* $p \leq .05$.
** $p \leq .01$.
*** $p \leq .001$.

56% of NCE sexually experienced adolescents engaged in sexual risk behaviors. Table 3 summarizes bivariate correlations among observed variables included in the path model.

3.2. Model estimation

Fig. 1 represents the final structural equation model-based multivariate path model resulting from iterative model-fitting procedures. Our initial model included: (1) paths from PCE (average summary score) to all four endogenous variables (externalizing behavior, substance use, early sexual intercourse, and sexual risk behavior); (2) paths from externalizing behavior to the other three endogenous variables; (3) paths from substance use latent variables and early sexual intercourse to sexual risk behavior; (4) a correlation between substance use and early sexual intercourse; and (5) paths from each exogenous variable (sex, violence exposure, home environment, and sexual victimization) to each of the four endogenous variables, creating a saturated model. Correlations were assumed for all exogenous variables in the model. This initial model produced a good fit, χ^2 (16) = 20.35, $p = .20$, CFI = .995, TLI = .985, RMSEA = .029 (90% CI = .000–.063), WRMR = .449. In order to achieve a more parsimonious model and to minimize the number of parameters that were estimated, paths coefficients with significance level of $p \geq .15$ were set to 0 (Hosmer and Lemeshow, 2000), producing insignificant differences, χ^2 (27) = 31.97, $p = .23$, CFI = .994, TLI = .990, RMSEA = .021 (90% CI = .000–.052), WRMR = .695, $\Delta\chi^2$ (11) = 12.91, $p = .30$. We also evaluated the relative fit of the full-mediation model (i.e., no direct path from PCE to sexual risk behavior), yielding a significant decrease in fit compared with the reduced partial mediation model, χ^2 (28) = 37.48, $p = .11$, CFI = .988, TLI = .981, RMSEA = .033 (90% CI = .000–.058), WRMR = .765, $\Delta\chi^2$ (1) = 5.53, $p = .02$. Thus, the partial mediation model was supported and was selected as the final path model (Fig. 1).

All paths reported in Fig. 1 were significant except the one path from externalizing behavior to substance use ($\beta = .12$, $p = .10$), after adjusting for gender, home environment, violence exposure, and sexual victimization. Fig. 1 shows two pathways from PCE to adolescent sexual risk behaviors: (1) direct effect of PCE on sexual risk behavior ($\beta = .16$, $p = .02$); and (2) PCE is related to greater externalizing behavior at age 12 ($\beta = .14$, $p = .009$) and, in turn, predicts early sexual intercourse ($\beta = .16$, $p = .03$), leading to later sexual risk behaviors ($\beta = .44$, $p < .001$). However, bootstrapping indicated a non-significant indirect effect ($\beta = .01$, 95% CI = −.002 to .022, $p = .18$). Substance use was correlated ($r = .60$, $p < .001$) with early sexual intercourse and predicted sexual risk behavior ($\beta = .31$, $p = .01$). Boys and poor home environment were related to earlier sexual intercourse. Greater violence exposure and sexual victimization were related to more externalizing behavior problems, substance use, and early sexual intercourse. Including preschool blood lead level in the path model did not change the effect of PCE, the effects of proposed mediators (externalizing behavior, substance use, and early sexual intercourse), or interrelationships among variables. Yet, higher lead level was related to early sexual intercourse ($\beta = .22$, $p = .005$). Due to the absence of changes in the effect of PCE on exogenous variables and reduced sample size, the path model without lead was presented. Approximately 49% of the total variation in sexual risk behavior was accounted for by the final model.

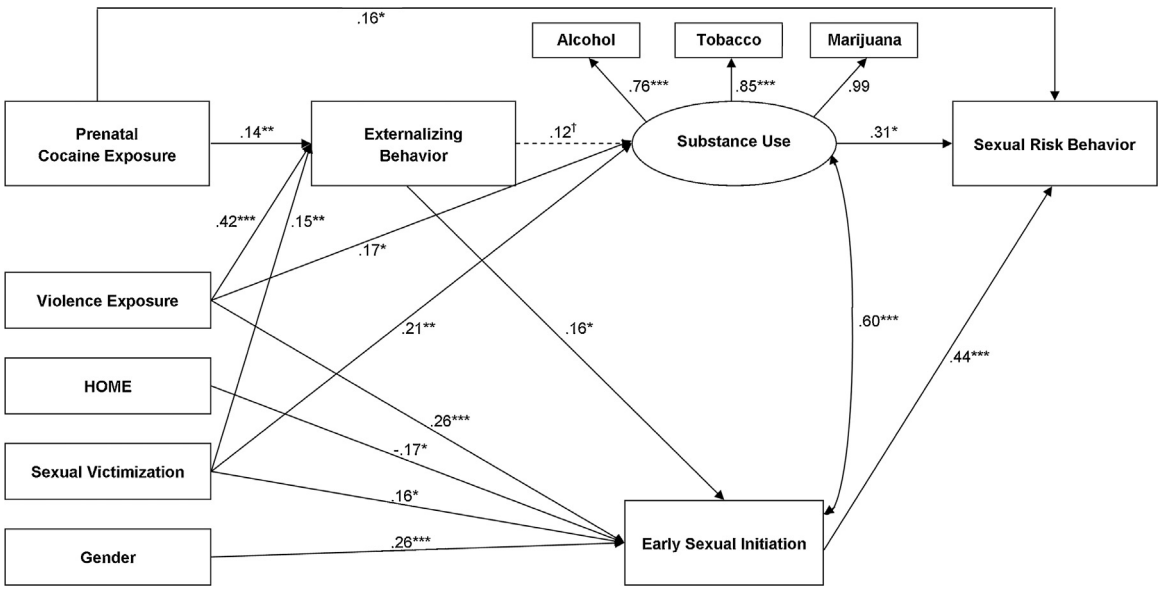

Fig. 1. The impact of prenatal cocaine exposure on adolescent sexual risk behaviors. Rectangles indicate observed variables, and oval represents latent constructs. All path coefficients are standardized. χ^2 (27) = 31.97, p = .23, CFI = .99, TLI = .99, RMSEA = .021 (90% CI = .000–.052), WRMR = .695. $^{\dagger}p \leq .10$, $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

4. Discussion

The present study extends previous findings by examining the effects of PCE on sexual risk behaviors assessed at ages 15 and 17. To our knowledge, this is one of the first studies to examine the prospective associations among PCE, preadolescence externalizing behaviors, adolescent substance use, early sexual behaviors, and sexual risk behavior simultaneously controlling for relevant confounders. Higher amount of PCE was related to more engagement in sexual risk behavior. The significant direct path, adjusting for covariates and possible mediators, may reflect a long-lasting effect of PCE. Although individual paths from PCE to externalizing behavior at age 12, to early sexual intercourse, and to later sexual risk behaviors by age 17 were all significant, the overall indirect effect did not reach significance. Three studies examined childhood/preadolescence behavioral adjustment and/or substance use as mediators of PCE on early sexual behavior. De Genna et al. (2014) reported that the effect of PCE on early sexual behavior was fully mediated by marijuana and alcohol use prior to age 15, but not by caregiver-reported externalizing behavior at age 7. Another prospective study (Lambert et al., 2013) reported that the effect of PCE on oral sex before age 15 was partially mediated by caregiver-reported attention problems at age 13. We also reported that the effect of PCE on early (<age 15) sexual intercourse was fully mediated by self-reported externalizing behavior at age 12 in girls, but not in boys (Min et al., 2015). These somewhat inconsistent findings may reflect methodological differences among studies in measuring mediators, ages when the mediators were assessed, and confounders adjusted, with different operationalization used in assessing confounders, all of which, nevertheless, collectively suggest non-ignorable impairment resulting from PCE.

Our study also demonstrated the global impact of adversity, indexed as violence exposure and sexual victimization, which was pervasive across ages, affecting externalizing behavior, early sexual behavior, and substance use. Adverse environments result in neurostructural changes, including reduction of the hippocampus and corpus callosum, and have consistently been associated with the development of behavioral problems, substance use, and psychopathology (Buckingham-Howes et al., 2013; Keyes et al., 2011; Senn et al., 2008). Given that PCE often co-occurs with adverse environments, understanding the role of adversity in the context of PCE, as an additive, independent risk or a moderator exacerbating the effect of PCE, will extend our knowledge of the effects of PCE.

Limitations in our study should be noted. In measuring sexual risk behavior, the number of items and response category (yes/no) did not allow for a more detailed account of risk behaviors. Participants' endorsement of "made someone pregnant" is limited to the pregnancies that participants were aware of and willing to report. Similarly, assessment of sexual risk behaviors relied on adolescents' self-report, subject to recall error and social desirability bias, as is the case of maternal/caregivers' self-report on prenatal and postnatal substance use. These two factors may underestimate the effects of PCE on sexual risk behaviors. The relatively small sample size for WLSMV precluded us from addressing possible gender variations in the path model using multiple group analysis, forcing us to treat gender as a covariate in the analysis. The sample composition limits generalizability of the findings to low-income, urban, predominantly African–American adolescents. Finally, our observational design cannot rule out that the apparent effects of PCE could be attributable to unmeasured genetic factors (D'Onofrio et al., 2013). Nevertheless, the present study has multiple strengths including the prospective design, assessment of a large number of adolescents and caregivers since birth with 90% retention, use of biological measures to classify exposure status as well as adolescent substance use, a large number of covariates evaluated including violence exposure, sexual victimization, and blood lead levels, and simultaneous evaluation of multiple mediators and their interrelationships.

In conclusion, adolescents with PCE were more likely to engage in risky sexual behavior by age 17, supporting the hypothesis of a persistent effect of PCE on behavior. Continued studies into adulthood will elucidate whether the childhood behavioral problems and early indications of substance use and sexual risk behavior in adolescence persist through early adulthood and affect social and vocational adjustment.

Conflict of interest

No conflict of interest declared.

Contributors

Dr. Meeyoung Min conceptualized the paper, performed the statistical analyses, and drafted the manuscript. Dr. Sonia Minnes designed the study and interpreted the data. Dr. Adelaide Lang coordinated the study, performed the measurements, and proofread the manuscript. Dr. Jeffrey Albert participated in the interpretation of data and helped to draft the manuscript. Ms. June-Yung Kim assisted in the literature review, drafting, and proofing the manuscript. Dr. Lynn Singer participated in the study's conception and design, interpretation of data, and reviewed the manuscript. All authors read and approved the final manuscript.

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References

Achenbach, T.M., Rescorla, L., 2001. Manual for the ASEBA School-Age Forms and Profiles. University of Vermont, Research Center for Children, Youth, and Families, Burlington, VT.

Ackerman, J.P., Riggins, T., Black, M.M., 2010. A review of the effects of prenatal cocaine exposure among school-aged children. Pediatrics 125, 554–565.

Buckingham-Howes, S., Berger, S.S., Scaletti, L.A., Black, M.M., 2013. Systematic review of prenatal cocaine exposure and adolescent development. Pediatrics 131, e1917–e1936.

Caldwell, B., Bradley, R.H., 2003. HOME Inventory Early Adolescent Version. University of Arkansas for Medical Sciences, Little Rock, AR.

CDC, 2009. YRBSS: Youth Risk Behavior Surveillance System. (http://www.cdc.gov/HealthyYouth/yrbs/index.htm (accessed on 29.12.12.).

CDC, 2012. Estimated HIV Incidence In the United States 2007–2010. HIV Surveillance Supplemental Report. 17 (No. 4). (http://www.cdc.gov/hiv/topics/surveillance/resources/reports/#supplemental (accessed on 17.07.15.).

CDC, 2014. Sexually Transmitted Disease Surveillance 2013. U.S. Department of Health and Human Services, Atlanta.

De Genna, N., Goldschmidt, L., Richardson, G.A., 2014. Prenatal cocaine exposure and age of sexual initiation: direct and indirect effects. Drug Alcohol Depend. 145, 194–200.

Derogatis, L., 1992. The Brief Symptom Inventory (BSI): Administration, Scoring and Procedures Manual II. Clinical Psychometric Research, Townson, MD.

D'Onofrio, B.M., Lahey, B.B., Turkheimer, E., Lichtenstein, P., 2013. Critical need for family-based quasi-experimental designs in integrating genetic and social science research. Am. J. Public Health 103, S46–S55.

Elkington, K.S., Bauermeister, J.A., Zimmerman, M.A., 2011. Do parents and peers matter? A prospective socio-ecological examination of substance use and sexual risk among African American youth. J. Adolesc. 34, 1035–1047.

Forhan, S.E., Gottlieb, S.L., Sternberg, M.R., Xu, F., Datta, S.D., McQuillan, G.M., Berman, S.M., Markowitz, L.E., 2009. Prevalence of sexually transmitted infections among female adolescents aged 14 to 19 in the United States. Pediatrics 124, 1505–1512.

Frank, D.A., Rose-Jacobs, R., Crooks, D., Cabral, H.J., Gerteis, J., Hacker, K.A., Martin, B., Weinstein, Z.B., Heeren, T., 2011. Adolescent initiation of licit and illicit substance use: impact of intrauterine exposures and post-natal exposure to violence. Neurotoxicol. Teratol. 33, 100–109.

Goldenberg, D., Telzer, E.H., Lieberman, M.D., Fuligni, A., Galván, A., 2013. Neural mechanisms of impulse control in sexually risky adolescents. Dev. Cognit. Neurosci. 6, 23–29.

Goldschmidt, L., Day, N.L., Richardson, G.A., 2000. Effects of prenatal marijuana exposure on child behavior problems at age 10. Neurotoxicol. Teratol. 22, 325–336.

Hamby, S.L., Finkelhor, D., Ormrod, R.K., Turner, H.A., 2004. The Juvenile Victimization Questionnaire (JVQ) Administration and Scoring Manual. Crimes Against Children Research Center, Durham, NH.

Hosmer, D.W., Lemeshow, S., 2000. Applied Logistic Regression. John Wiley & Sons, Inc., New York.

Hu, L., Bentler, P.M., 1998. Fit indices in covariance structure modeling: sensitivity to underparameterized model misspecification. Psychol. Methods 3, 424–453.

Kann, L., Kinchen, S., Shanklin, S.L., Flint, K.H., Kawkins, J., Harris, W.A., Lowry, R., Olsen, E., McManus, T. Chyen, D., 2014. Youth risk behavior surveillance—United States 2013, MMWR Surveill Summ., 63, (No. SS-4), 1–168.

Keyes, K.M., Hatzenbuehler, M.L., Hasin, D.S., 2011. Stressful life experiences, alcohol consumption, and alcohol use disorders: the epidemiologic evidence for four main types of stressors. Psychopharmacology 218, 1–17.

Kosofsky, B.E., Wilkins, A.S., Gressens, P., Evrard, P., 1994. Transplacental cocaine exposure: a mouse model demonstrating neuroanatomic and behavioral abnormalities. J. Child Neurol. 9, 234–241.

Khurana, A., Romer, D., Betancourt, L.M., Brodsky, N.L., Giannetta, J.M., Hurt, H., 2012. Early adolescent sexual debut: the mediating role of working memory ability sensation seeking, and impulsivity. Dev. Psychol. 48, 1416–1428.

Lambert, B.L., Bann, C.M., Bauer, C.R., Shankaran, S., Bada, H.S., Lester, B.M., Whitaker, T.M., Lagasse, L.L., Hammond, J., Higgins, R.D., 2013. Risk-taking behavior among adolescents with prenatal drug exposure and extrauterine environmental adversity. J. Dev. Behav. Pediatr. 34, 669–679.

Lane, S.D., Webster, N.J., Levandowski, B.A., Rubinstein, R.A., Keefe, R.H., Wojtowycz, M.A., Cibula, D.A., Kingson, J.E.F., Aubry, R.H., 2008. Environmental injustice: childhood lead poisoning, teen pregnancy, and tobacco. J. Adolesc. Health 42, 43–49.

Larkby, C.A., Goldschmidt, L., Hanusa, B.H., Day, N.L., 2011. Prenatal alcohol exposure is associated with conduct disorder in adolescence: findings from a birth cohort. J. Am. Acad. Child Adolesc. Psychiatry 50, 262–271.

McCarthy, D.M., Kabir, Z.D., Bhide, P.G., Kosofsky, B.E., 2014. Effects of prenatal exposure to cocaine on brain structure and function. Prog. Brain Res. 211, 277–289.

Maughan, B., Taylor, A., Caspi, A., Moffitt, T.E., 2004. Prenatal smoking and early childhood conduct problems: testing genetic and environmental explanations of the association. Arch. Gen. Psychiatry 61, 836–843.

Min, M.O., Singer, L.T., Kirchner, H.L., Minnes, S., Short, E., Hussain, Z., Nelson, S., 2009. Cognitive development and low-level lead exposure in poly-drug exposed children. Neurotoxicol. Teratol. 31, 225–231.

Min, M.O., Minnes, S., Lang, A., Weishampel, P., Short, E.J., Yoon, S., Singer, L.T., 2014a. Externalizing behavior and substance use related problems at 15 years in prenatally cocaine exposed adolescents. J. Adolesc. 37, 269–279.

Min, M.O., Minnes, S., Yoon, S., Short, E.J., Singer, L.T., 2014b. Self-reported adolescent behavioral adjustment: effects of prenatal cocaine exposure. J. Adolesc. Health 55, 167–174.

Min, M.O., Minnes, S., Lang, A., Yoon, S., Singer, L.T., 2015. Effects of prenatal cocaine exposure on early sexual behavior: gender difference in externalizing behavior as a mediator. Drug Alcohol Depend. 153, 59–65.

Minnes, S., Singer, L.T., Kirchner, H.L., Short, E., Lewis, B., Satayathum, S., Queh, D., 2010. The effects of prenatal cocaine exposure on problem behavior in children 4–10 years. Neurotoxicol. Teratol. 32, 443–451.

Minnes, S., Singer, L., Min, M.O., Wu, M., Lang, A., Yoon, S., 2014. Effects of prenatal cocaine/polydrug exposure on substance use by age 15. Drug Alcohol Depend. 134, 201–210.

Muthén, L.K., Muthén, B.O., 2012. Mplus User's Guide, Seventh edition. Muthén & Muthén, Los Angeles, CA.

Preacher, K.J., Hayes, A.F., 2008. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav. Res. Methods 40, 879–891.

Ramrakha, S., Bell, M.L., Paul, C., Dickson, N., Moffitt, T.E., Caspi, A., 2007. Childhood behavior problems linked to sexual risk taking in young adulthood: a birth cohort study. J. Am. Acad. Child Adolesc. Psychiatry 46, 1272–1279.

Richardson, G.A., Larkby, C., Goldschmidt, L., Day, N.L., 2013. Adolescent initiation of drug use: effects of prenatal cocaine exposure. J. Am. Acad. Child Adolesc. Psychiatry 52, 37–46.

Ridenour, T.A., Clark, D.B., Cottler, L.B., 2009. The illustration-based assessment of liability and exposure to substance use and antisocial behavior for children. Am. J. Drug Alcohol Abuse 35, 242–252.

Senn, T.E., Carey, M.P., Vanable, P.A., 2008. Childhood and adolescent sexual abuse and subsequent sexual risk behavior: evidence from controlled studies methodological critique, and suggestions for research. Clin. Psychol. Rev. 28, 711–735.

Singer, L.T., Minnes, S., Short, E., Arendt, R., Farkas, K., Lewis, B., Klein, N., Russ, S., Min, M.O., Kirchner, H.L., 2004. Cognitive outcomes of preschool children with prenatal cocaine exposure. JAMA 291, 2448–2456.

Singer, L.T., Nelson, S., Short, E., Min, M.O., Lewis, B., Russ, S., Minnes, S., 2008. Prenatal cocaine exposure: drug and environmental effects at 9 years. J. Pediatr. 153, 105–111.

SAMHSA, 2014. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-49, HHS Publication No. SMA 14-4863, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Thompson, B.L., Levitt, P., Stanwood, G.D., 2009. Prenatal exposure to drugs: effects on brain development and implications for policy and education. Nat. Rev. Neurosci. 10, 303–312.
Warner, T.D., Behnke, M., Eyler, F.D., Szabo, N.J., 2011. Early adolescent cocaine use as determined by hair analysis in a prenatal cocaine exposure cohort. Neurotoxicol. Teratol. 33, 88–99.
Wechsler, D., 2003. Wechsler Intelligence Scale for Children—Fourth Edition (WISC-IV), Fourth edition. The Psychological Corporation, San Antonio, TX.
Wu, J., Witkiewitz, K., McMahon, R.J., Dodge, K.A., 2010. Conduct problems prevention research group, a parallel process growth mixture model of conduct problems and substance use with risky sexual behavior. Drug Alcohol Depend. 111, 207–214.
Yu, C.Y., Muthén, B.O., 2002. Evaluation of Model Fit Indices for Latent Variable Models with Categorical and Continuous Outcomes (Technical Report). UCLA Graduate School of Education and Information Studies, Los Angeles.