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Prenatal drug exposure, behavioral problems and drug experimentation among African American urban adolescents

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Abstract

Purpose—To examine how prenatal heroin/cocaine exposure (PDE) and behavioral problems relate to adolescent drug experimentation.

Methods—The sample included African American adolescents (mean age=14.2 yr, SD=1.2) with PDE (n=73) and a non-exposed community comparison (n=61). PDE status was determined at delivery through toxicology analysis and maternal-report. Internalizing/externalizing problems were assessed during adolescence with the Behavior Assessment System for Children, Second Edition. Drug experimentation was assessed by adolescent-report and urine analysis. Logistic regression evaluated the likelihood of drug experimentation related to PDE and behavioral problems, adjusting for age, gender, prenatal tobacco/alcohol exposure, perceived peer drug use and caregiver drug use. Interaction terms examined gender modification.

Results—67 (50%) used drugs. 25 (19%) used tobacco/alcohol only and 42 (31%) used marijuana/illegal drugs. 94 (70%) perceived peer drug use. PDE significantly increased the risk of tobacco/alcohol experimentation (OR=3.07, 95% CI: 1.09–8.66, p=0.034), but not after covariate adjustment (aOR=1.31, 95% CI: 0.39–4.36, p>0.05). PDE was not related to overall or marijuana/illegal drug experimentation. The likelihood of overall drug experimentation was doubled per Standard Deviation (SD) increase in externalizing problems (aOR=2.28, 95% CI: 1.33–3.91, p=0.003) and, among girls, 2.82 times greater (aOR=2.82, 95% CI: 1.34–5.94, p=0.006) per SD increase in internalizing problems. Age and perceived peer drug use were significant covariates.

Conclusions—Drug experimentation was relatively common (50%), especially in the context of externalizing problems, internalizing problems (girls only), age, and perceived peer drug use.

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Findings support Problem Behavior Theory and suggest that adolescent drug prevention address behavioral problems and promote prosocial peer groups.

Keywords

drug experimentation; prenatal drug exposure; behavioral problems; gender

Prenatal drug exposure to heroin/cocaine (PDE) is a public health problem, reported by 4.4% of pregnant women and increasing to 7.7% among African American women [1]. PDE increases the risk for behavioral problems during childhood and adolescence [2]. Studies among children without PDE [3] have found that behavioral problems during childhood increase the risk for adolescent drug experimentation. Thus, behavioral problems among children with PDE may be an early sign of risk for drug experimentation.

Adolescence provides a unique opportunity to examine how PDE relates to problem behaviors and drug experimentation. Not only is adolescence characterized by increasingly complex cognitive abilities and expectations, but risk-taking behaviors escalate during adolescence [4]. Young adolescents who engage in early drug experimentation are at risk for ongoing drug use and dependence in adulthood [5].

We searched PubMed, PsycInfo, Web of Science, and CINAHL databases with terms “prenatal drug, substance, or cocaine exposure; in utero substance/drug exposure; adolescence/adolescent; and substance/drug use” in May 2013, and identified six papers published on PDE and adolescent drug experimentation (Table 1). All were published since 2006, indicating that this is a new area of investigation. Most were conducted among low-income African American adolescents. Two studies among early adolescents (11–12.5 years) found low rates of drug use and no PDE-drug experimentation association [6,7]. One study among middle adolescents (14 years) reported an association between PDE and cocaine use [8]. Three studies among late adolescents (15–16 years) found mild-moderate associations between PDE and drug experimentation [9, 10]. One study [11] found that after controlling for neurobehavioral disinhibition during childhood, PDE was not associated with adolescent drug use, suggesting a pathway to drug use through childhood behavioral problems. However, another study [10] reported that neither late adolescent depressive symptoms nor externalizing problems mediated the effect of PDE on adolescent drug use.

Animal research suggests that the effect of PDE on nigrostriatal dopamine neuronal function is stronger for males than females [12], raising the possibility of gender variation in PDE-drug experimentation. Only one of the six studies of adolescent drug experimentation examined gender differences and found no gender variation [7]. In summary, drug experimentation among adolescents with a PDE history increases with age. The one study conducted in mid-adolescence reported a relatively high prevalence of adolescent cocaine experimentation (29%) [8], compared to the studies conducted among older adolescents [11]. In addition, several studies relied exclusively on self-report, with limited attention to mechanisms or gender variation.

This study examines how PDE relates to drug experimentation during mid-adolescence using self-report and physiological measures, while focusing on mechanisms and gender

variation, guided by Problem Behavior Theory (PBT, [13]). PBT is a psychosocial model that explains behavioral outcomes such as drug use in adolescence. It describes three independent but related systems of psychosocial components: (1) the personality system including motivation, personal beliefs, and personal controls; (2) the perceived environmental system, such as perceived support or influence from parents and friends; and (3) the behavior system, consisting of a problem behavior structure and a conventional behavioral structure. PBT suggests that a connection between externalizing behavior problems and adolescent drug use may be manifestations of an underlying construct of unconventionality. We tested three hypotheses: 1) PDE increases the likelihood of drug experimentation; 2) adolescents with problem behaviors are at increased risk for drug experimentation, particularly among the PDE group; and 3) the relationship between PDE, problem behaviors, and drug experimentation varies by gender and age. Perceived peer and caregiver drug use represent the perceived environment of PBT, and socio-demographic characteristics, and prenatal tobacco and alcohol exposure have been associated with adolescent drug experimentation [14–17]. All were included as covariates.

Methods

Participants

Data are from a prospective study of adolescents. The PDE sample was recruited at birth. Eligibility included gestational age ≥ 32 weeks, birth weight ≥ 1,750 grams, no neonatal intensive care unit admission, and cocaine and/or heroin exposure based on maternal and/or infant urine toxicology and/or maternal self-report of cocaine and/or heroin use during pregnancy. All adolescents in the PDE group were prenatally exposed to cocaine and/or heroin and 86% were also prenatally exposed to tobacco and/or alcohol. Families were randomized to an intervention group that received developmentally oriented home visits or a control group that received monthly tracking visits for 1 year [18]. The non-exposed (NE) community comparison group was recruited during middle childhood and adolescence from a primary care clinic. Medical records were reviewed to identify children born at the same hospital and during the same years as the PDE group. Eligibility included negative maternal and infant toxicology screens for cocaine/heroin, no maternal report of substance use, no medical chart indication of cocaine/heroin use, and residence in the same community as the PDE group. Groups were matched for maternal education, age of first pregnancy, child age, gender, and race. The University's Institutional Review Board approved the study. All caregivers and youth provided written consent or assent. Participants were followed through middle adolescence. Adolescents and caregivers were evaluated in a laboratory setting using audio computer-assisted self-interview (ACASI). Evaluators were unaware of exposure history. Except for PDE, all variables were assessed during adolescence.

Adolescents were 50% male, 99% African-American, 14.2 years of age (SD=1.2), and 54% were PDE (Table 2).

Measures

Dependent variable

Drug Experimentation: Adolescents provided a urine sample and completed the Adolescent Health Behavior Survey, adapted from the YRBS, containing questions about tobacco, alcohol, marijuana, glue, inhalants, steroids, prescription drugs, cocaine, heroin, "club drugs," amphetamines, and injection drugs [19]. The urine sample was tested for amphetamines/methamphetamines, barbiturates, benzodiazepines, cocaine, marijuana, methadone, opiates, PCP, propoxyphene, and tricyclic antidepressants using the Fischer Scientific Triage Drugs of Abuse Panel. Participants were defined as "experimenters" if they indicated any drug use or their urine test was positive. Adolescents who denied drug use and had a negative urine test were defined as "abstainers." Two subtype variables were created: (1) experimentation with tobacco and/or alcohol only, but no marijuana or other illegal drugs, (2) experimentation with marijuana and/or other illegal drugs, regardless of tobacco/alcohol use. Both were compared to no experimentation with any drugs.

Independent variables

PDE: PDE was defined as positive maternal and/or infant urine toxicology or maternal report or medical record indication of cocaine and/or heroin use during pregnancy. NE was defined as negative for both maternal and infant toxicology, and no medical record or maternal report of cocaine and/or heroin use. Heavy PDE (84%, n=61) was defined as cocaine and/or heroin use during pregnancy 2 or more times/week, and light PDE as use less than 2 times/week. Since heavy/light exposure did not differ in adolescent drug experimentation, we combined them in analyses.

Behavior problems: Behavior problems were assessed with the Behavior Assessment System for Children, Second Edition (BASC-2) [20]. Raw scores were used as recommended by the BASC-2 developers and were computed by summing adolescent-reported internalizing problems and caregiver-reported externalizing problems, with higher scores indicating more problems. Cronbach's alpha was 0.92 for externalizing behaviors and 0.91 for internalizing behaviors.

Covariates

Prenatal tobacco and alcohol exposure (PTE, PAE): The PDE group reported use at delivery and the NE group at enrollment. Two dichotomous variables were created: tobacco exposure (yes/no) and alcohol exposure (yes/no).

Perceived peer drug use: Four questions from the Adolescent Health Behavior Survey assessed perceived peer drug use, such as "The kids I hang around with do not use alcohol, marijuana, or other drugs" using a 4-point Likert scale. Responses were categorized as "perceived use" (agree/strongly agree that peers used drugs for at least one question) and "no perceived use" (disagree/strongly disagree that peers used drugs for all questions).

Caregiver drug use: Caregivers responded to 13 questions about drug use including being drunk, using marijuana, cocaine, heroin, or other type of illegal drugs in the past 30 days.

Caregivers were mothers (79%), grandparents (10.4%), aunt/uncle (4.5%), father (2.2%), sibling (1.5%), step/foster parents (1.4%), or others (1%). Caregiver relationship was not related to drug experimentation. Caregivers were categorized as "current users" if they responded affirmatively to at least one question and as "non-current users" otherwise.

Family stress: Food security indicating family stress [21] was measured with the U.S. Department of Agriculture's Food Security Scale [22]. Caregivers responded to 18 questions about food security within the last year. Families were categorized as food secure (0–2 affirmative responses), and insecure (3–18 affirmative responses) [22].

Neighborhood safety: Caregivers responded to five questions from the Neighborhood Questionnaire regarding drugs, crime, and police protection using a 4 or 5-point Likert scale [23]. The mean score was calculated; high scores indicated more safety. Cronbach's alpha was 0.75.

Intervention: We tested the direct effect of intervention status on adolescent drug experimentation, the mediated effect via maternal drug use, and the moderated effect by intervention or maternal depressive symptoms on PDE-drug experimentation. There were no significant findings, and intervention status was not included in the analyses.

Statistical analysis

T-tests, chi-square tests and Fisher's exact tests compared sample characteristics by PDE, gender, and drug experimentation. Logistic regression (LR)estimated the odds ratio (OR) of overall drug experimentation for PDE and behavioral problems before and after covariate adjustment, with separate models for internalizing (Model 1) and externalizing problems (Model 2) to avoid collinearity. The LR was repeated using the two subtype drug experimentation as outcome variables, separately. To examine the synergistic effect of PDE and behavior problems, we included the PDE by behavior problems interaction term. To examine whether gender/age modified the relationships between PDE (or behavioral problems) and drug experimentation, we included the interaction between gender/age and PDE (or behavioral problems), separately. If significant, we stratified the models by gender/age group. Exact logistic regression, designed for small cell sizes, was compared to LR [24]. Results were similar, so we reported LR results. SPSS 20.0, and SAS 9.2 were used.

Results

Half of the youth (n=67, 50%, Table 2) experimented with at least one drug, including 28% tobacco, 31% alcohol, 23% marijuana, and 11% other drugs (e.g., glue or non-medical prescription drugs). Sixty-five youth self-reported drug use (49%), and 7 had a positive urine test (5%, 1 amphetamines, and 6 marijuana) including 2 who denied self-reported drug use. None used "club drugs," heroin, cocaine, or injection drugs. Twenty-five (19%) used tobacco/alcohol only, and 42 (31%) used marijuana/illegal drugs. Most (70%) perceived peer drug use.

Half (50%) of the caregivers reported food insecurity; 26% reported fairly/very often problems with crime, and 46% reported fairly/very serious problems with neighborhood

drugs. Neither food security nor neighborhood safety was significantly related to either PDE/NE or to overall/subtype drug experimentation. They were removed from analyses, but the information was retained in the method to characterize the context of the sample.

Bivariate analyses by PDE status

PDE and NE groups did not differ in overall drug experimentation (53% PDE vs. 46% NE, p=0.386, Table 2). The prevalence of tobacco/alcohol experimentation differed between PDE and NE group (26% vs. 10%, p=0.035), but marijuana/illegal drug experimentation did not differ by PDE (p>0.05).

PDE group had higher internalizing scores (371.9 vs. 345.6, p=0.010), PTE (78% vs. 21%, p<0.001), PAE (53% vs. 18%, p<0.001), and marginally greater caregiver drug use (14% vs. 5%, p=0.084) than NE group. PDE and NE groups did not differ in gender, externalizing scores, perceived peer drug use, or age.

Bivariate analyses by gender

No gender differences were found in overall drug experimentation (49% vs. 51%, p=0.863), tobacco/alcohol experimentation, marijuana/illegal drug experimentation, PDE, internalizing or externalizing problems, or any covariate (Table 2).

Bivariate analyses by overall drug experimentation

Adolescents who experimented with drugs had significantly higher externalizing (162.8 vs. 147.3, p=0.001), internalizing scores (370.0 vs. 349.2, p=0.042) and older age (14.4 vs. 13.9, p=0.022) than abstainers (Table 3). The prevalence of overall drug experimentation was higher among adolescents with perceived peer drug use than those without perceived peer drug use (60% vs. 28%, p=0.001) and marginally higher among adolescents with caregiver drug use than those without caregiver drug use (77% vs. 48%, p=0.077). It was not associated with gender, PDE, PTE, or PAE (ps>0.05).

Logistic regression for overall drug experimentation

PDE was not related to overall drug experimentation either before or after covariate adjustment (ps>0.1) (Table 3). The likelihood of drug experimentation was increased by 2.28 times per SD higher externalizing score (adjusted OR, aOR=2.28, 95% CI: 1.33–3.91, p=0.003) and marginally by 1.47 times per SD higher internalizing score (aOR=1.47, 95% CI: 0.96–2.27, p=0.079). Drug experimentation was positively related to perceived peer drug use, older age, marginally to caregiver drug use (not significant after covariate adjustment), but not gender, PTE, or PAE. There was no significant interaction between PDE and behavior problems (either externalizing or internalizing).

There was a significant interaction between gender and internalizing problems (p=0.003). Other interactions between age/gender and PDE/behavioral problems were not significant. Stratified analyses by gender showed that, the likelihood of drug experimentation was increased almost threefold per SD higher internalizing score among girls (aOR=2.82, 95% CI: 1.34–5.94, p=0.006, Table 5), but not boys.

Logistic regression for subtype drug experimentation

Two separate LR models were conducted for tobacco/alcohol experimentation versus no experimentation with any drug (n=92, excluding 42 adolescents who ever used marijuana/illegal drugs), and marijuana/illegal drug experimentation versus no experimentation with any drug (n=109, excluding 25 adolescents who used tobacco/alcohol only). PDE significantly increased the likelihood of tobacco/alcohol experimentation (OR=3.07, 95% CI: 1.09–8.66, p=0.034), but not after covariate adjustment (ps>0.05, Table 4). To examine the mechanisms, we conducted step-wise hierarchical analyses with age, gender, PAE, and PTE (step 1), caregiver and peer drug use (step 2), and internalizing or externalizing problems (step 3). PDE was not related to tobacco/alcohol experimentation after PTE adjustment. Instead, PTE increased the likelihood of experimentation by 11 times even after adjusting for PDE and other variables (aOR=11.21, 95% CI: 2.40–52.35, p=0.002).

Regarding behavior problems, the likelihood of tobacco/alcohol experimentation was increased by 2.38 times per SD higher externalizing score (aOR=2.38, 95% CI: 1.05–5.37, p=0.037) and marginally by 1.82 times per SD higher internalizing score (aOR=1.82, 95% CI: 0.97–3.41, p=0.060, Table 4). There was no significant interaction between PDE and behavior problems (either externalizing or internalizing).

Only the gender by internalizing problems interaction was significant (p=0.008). No other interactions between gender/age and PDE/behavior problems were significant. The likelihood of tobacco/alcohol experimentation was increased almost fourfold per SD higher internalizing score (aOR=3.88, 95% CI: 1.30–11.53, p=0.015, Table 5) among girls, not boys.

PDE was not related to marijuana/illegal drug experimentation. The likelihood of marijuana/illegal drug experimentation was increased by 2.65 times per SD higher externalizing score (aOR=2.65, 95% CI: 1.40–5.02, p=0.003), but not internalizing score (p>0.05). There was no significant interaction between PDE and behavior problems (either externalizing or internalizing).

Only the gender by internalizing problems interaction was marginally significant (p=0.072). No other interaction between gender/age and PDE/behavior problems was significant. One SD higher internalizing problems doubled the likelihood of marijuana/illegal drug experimentation (aOR=2.00, 95% CI: 0.93–4.30, p=0.078, Table 5) among girls, but not among boys.

Discussion

There are four primary findings related to PDE, problem behaviors, and adolescent drug experimentation. First, there was no evidence of a PDE-drug experimentation association by middle adolescence. Second, PDE was associated with internalizing problems, but not externalizing problems during adolescence. Third, adolescent drug experimentation was modestly associated with externalizing problems. Fourth, adolescent drug experimentation was modestly associated with internalizing problems among girls, but not boys.

Drug experimentation was relatively common (50%) in the sample, illustrating that drug experimentation is a serious concern among low-income urban mainly African American adolescents. However, there was no evidence that PDE increased the likelihood of drug experimentation by middle adolescence. This finding is consistent with two studies that found no association between PDE and drug experimentation during early adolescence [6,7]. The finding that in Detroit, PDE was associated with cocaine use among middle adolescents (age 14) [8] and the three studies that found a PDE-adolescent drug use relationship after age 15 [9–11], suggest that PDE is not a risk factor for drug experimentation in early adolescence, but may begin to emerge in middle adolescence. Our finding that age is an independent predictor of adolescent drug experimentation, regardless of PDE, provides additional evidence on the role of increasing adolescent age in drug experimentation. PDE was related to higher levels of tobacco/alcohol experimentation in the crude model, but the relationship was non-significant after PTE adjustment , suggesting that PTE, rather than PDE, increased the risk of adolescent tobacco/alcohol experimentation. This result is consistent with a longitudinal finding that PTE increases the risk of nicotine dependence among adolescent girls [16]. One possibility is that the high availability of household tobacco among tobacco-using caregivers may increase the risk for adolescents to experiment with tobacco/alcohol [25].

PDE was associated with internalizing, but not externalizing problems during adolescence. Findings regarding the PDE-adolescent problem behavior link have been mixed [26]. One study reported that girls in the PDE group reported more anxiety in response to stress than girls in the NE group [27]. One possibility is an association between PDE and the dopaminergic system [12] resulting in changes in the self-regulatory and reward systems [28,29]. It is plausible that alterations in these systems may lead to behavioral problems, disrupt social adjustment, and increase the likelihood of drug experimentation [30]. Further work is necessary to disentangle these potential associations.

Regardless of PDE, there was a modest association between externalizing problems and adolescent drug experimentation. These findings supported PBT, suggesting that both externalizing problems and drug use may reflect an underlying vulnerability for delinquent behavior, or general syndrome of deviance [13]. Drug experimentation was higher among adolescents who perceived peer drug use, consistent with the theorized role of the perceived environmental system on behavioral outcomes in PBT. The structural environment of the adolescents may also contribute to the understanding of drug experimentation among adolescents. The high rate of household food insecurity, together with neighborhoods characterized by frequent drug use and crime, provide a context that may increase stress for both caregivers and adolescents, potentially reducing family functioning [31]. Adverse neighborhood or familial factors may enable access to drugs [32]. With perceived peer drug use reported by a majority of adolescents (~70%), drug experimentation may be seen as a positive, and even desirable, option, in the face of daily stress in the low-income, urban mainly African American adolescents. Future research can integrate elements of PBT by including the protective elements of the environment, along with the personality system, including personal beliefs, values and goals [13].

Internalizing problems were positively related to drug experimentation among girls, but not boys. One possible explanation for this gender-specific finding may be related to coping strategies. Just as adult women demonstrate a stronger association between internalizing problems and alcohol dependence than men [33], girls may use passive, self-directed strategies, such as smoking tobacco or drinking alcohol to self-medicate mood or anxiety problems. Other explanations, such as differential physiological effects of drugs related to sex hormones cannot be excluded [34]. Our finding that the internalizing problems-drug experimentation relationship is stronger for tobacco/alcohol than marijuana/other illegal drugs is consistent with one study reporting that depressed mood in 6th graders predicted increases in tobacco/alcohol use over two years, but not marijuana use [35]. Smoking has antidepressant effects through inhibiting activity levels of monoamine oxidase (MAO), an enzyme involved in oxidizing serotonin, norepinephrine, and dopamine and associated with negative mood and depression [36].

This study has several methodological limitations. First, although we used statistical procedures designed for small sample sizes, the wide confidence intervals do not rule out the possibility of associations. Second, the relationship between behavioral problems and drug experimentation is contemporary; the data were collected concurrently during adolescence. Third, although PTE/PAE were collected using the same methods for PDE/NE groups, the timing differed, which may introduce recall bias. Finally, we could not fully apply PBT to our investigation, as we did not have a measure of the personality system.

This study has several methodological advantages and unique contributions. First, it includes a well characterized sample of adolescents with PDE followed from birth through middle adolescence and a NE comparison group. Second, two methods (self-report and urine analysis) were used to assess PDE and adolescent drug use. Third, the ACASI method for questions related to drug use may have increased response reliability by ensuring privacy [37]. Finally, PBT theory was used to investigate the mechanisms underlying drug experimentation.

Conclusion

This study contributes to the understanding of the PDE-drug experimentation relationship by middle adolescence. These results have important implications for adolescent drug use prevention, suggesting that preventive interventions need to take place among children with PDE prior to adolescence. The associations between adolescent drug experimentation with externalizing problems, and perceived peer drug use, are consistent with PBT. Adolescent drug experimentation is associated with internalizing problems among girls. These findings suggest that screening and helping adolescents reduce behavioral problems and providing interventions for girls with internalizing problems may prevent drug experimentation. The association between PDE and adolescent internalizing problems and the associated risk for mental health problems in adulthood [38], provide additional evidence for the importance of identifying and intervening among adolescents with PDE who experience internalizing problems. With additional studies, a meta-analysis can clarify the relationships and mechanisms between PDE and adolescent drug experimentation.

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Implications and Contribution

Among urban African-Americans, drug experimentation is high (50%) by middle adolescence, both for those with prenatal drug exposure and those without. Consistent with Problem Behavior Theory (PBT), drug experimentation was associated with externalizing problems and peer drug use and, for girls only, with internalizing problems. Findings support PBT and prevention of behavior problems to reduce drug experimentation.

Table 1

Comparison of six studies of prenatal exposure to heroin/cocaine (PDE) in relation to adolescent drug experimentation.

Author (Year)	Sample composition					PDE and measurement	Outcome (drug use) definition	Outcome measurement method	Prevalence of drug use	Internalizing / externalizing problems and related findings	Gender variation	Main PDE Finding	Effect size for PDE-drug use relation
	N	Age (yr)	Ethnicity (%)	SES	Gender (%)								
Lagasse, et al., 2006	517 (PDE= 44%)	11	83% AA	Low income, urban	NR	Mainly cocaine exposed, 8% opiates Self-report and meconium	Alcohol, tobacco, and illegal drug use	Self-report	NR	PDE not related to depression, ADHD, CD or ODD NR for relation between internalizing/ externalizing problems and drug use	NR	PDE was not related to drug use	NR
Delaney-Black, et al, 2011	316	14	100% AA	Low income, urban	50% male	Mainly cocaine exposed, some opiates Urine toxicology, meconium, self-report, medical records, and retrospective report	Cocaine, opiate, marijuana and alcohol use	Hair, sweat, urine test, teen self-report, parent report	29% cocaine use, 5% opiates use, 4% marijuana use	PDE not related to adolescent CD and PTSD Adolescent CD and PTSD not related to cocaine use.	Gender was not related to cocaine use	PDE was related to cocaine use	r=0.20 for prenatal cocaine exposure and teen cocaine use
Frank et al. 2011	149 (PDE= 54%)	16	85–93% AA	Low income, urban	44–54% male	Cocaine exposed (heavy, light, NE) Self-report, urine toxicology and meconium	Any drug use, marijuana, alcohol, and illegal drug use	Self-report, urine test	48–74% for any drug use	No difference in childhood externalizing behavior by PDE Childhood externalizing behavior included as covariate, but NR for its relationship with drug use	NR	Heavy PDE was related to initiation of any drug use, particularly marijuana and alcohol	HR=2.1 for heavy PDE vs. NE HR=1.2–1.4 for light PDE vs. NE
Lester et al., 2012	903 (PDE= 43%)	16	80–83% AA	Low-income	50–52% male	Cocaine exposed, some opiates Maternal report and	Alcohol, tobacco, marijuana, illegal drug, and any drug use	Self-report	11–16% tobacco use, 20–28% illegal drug use, 47% any	Childhood Neurobehavioral disinhibition (ND) score higher in NE than PDE.	NR	PDE was initially related to tobacco, marijuana and	OR=1.0–1.5 aOR=0.9–1.1

Author (Year)	Sample composition					PDE and measurement	Outcome (drug use) definition	Outcome measurement method	Prevalence of drug use	Internalizing / externalizing problems and related findings	Gender variation	Main PDE Finding	Effect size for PDE-drug use relation
	N	Age (yr)	Ethnicity (%)	SES	Gender (%)								
						meconium screens meconium screens			drug use	ND was related to initiation of alcohol, tobacco, illegal and any drug use, but not marijuana use. Time-varying ND related to all categories of drug initiation.		illegal drug initiation, but not after adjustment for ND and covariates	
Warner et al. 2011	263 (PDE= 49%)	12.5	81–83% AA	Low income, rural	44–50% male	Cocaine exposed Self-report and urine toxicology	Cocaine use	Hair test	3–5% for cocaine use	No difference in Childhood CBCL and YSR internalizing or externalizing problems by PDE Childhood CBCL externalizing problems and social problems related to cocaine use. CBCL Internalizing Problems, RCMAS, and CDI scores not related to drug use	Gender was not related to drug use; no gender variation in PDE effect on drug use	No evidence of PDE in relation to cocaine use.	aOR=0.70
Richard -son et al., 2013	214 (NR for PDE%)	15.3	50% AA	Median family income $2,.000 per month (range 0-$12,083)	52% male	Cocaine exposed (first, 2nd and third trimester), self-report	Tobacco, alcohol, marijuana initiation, lifetime and current use	Self-report	31–46% for alcohol use, 32–42% for tobacco use, 14–31% for past-year marijuana use	Depressive symptoms at age 10 predicted current alcohol use. Depressive symptoms and externalizing behavior problems at age 10 predicted tobacco initiation.	NR	PDE was related to initiation of alcohol and marijuana, and past-year marijuana use.	aHR=1.8

Author (Year)	Sample composition					PDE and measurement	Outcome (drug use) definition	Outcome measurement method	Prevalence of drug use	Internalizing / externalizing problems and related findings	Gender variation	Main PDE Finding	Effect size for PDE-drug use relation
	N	Age (yr)	Ethnicity (%)	SES	Gender (%)								
										No mediation effect of depressive No mediation effect of depressive No mediation effect of depressive symptoms or CBCL externalizing problem at age 10 on the relationship of PDE and drug use			

Note. PDE=Prenatal Heroin/cocaine Exposure; NR=Not Reported; NE=Non-Drug Exposed; AA=African American; SES=Socio-Economic Status ADHD=Attention Deficit Hyperactivity Disorder; CD= Conduct Disorder; ODD=Oppositional Deviance Disorder; PTSD= Post-Traumatic Stress Disorder; YRBSS=Youth Risk Behavior Surveillance System; HONC=Hooked on Nicotine Checklist; CBCL = Child Behavior Checklist; RCMAS=Revised Children's Manifest Anxiety Scale; CDI = Children's Depression Inventory; r=correlation coefficient; HR=Hazard Ratio; aHR=adjusted Hazard Ratio; OR=Odds Ratio; aOR=adjusted Odds Ratio.

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Table 2

Selected sample characteristics overall and stratified by gender and prenatal exposure to heroin/cocaine (PDE), separately (n=134).

	Total	NE * (n=61, 46%)	PDE** (n=73, 54%)	p ***	Girls (n=67, 50%)	Boys (n=67, 50%)	P***
Age (mean, SD)	14.2(1.2)	14.0(1.2)	14.3(1.2)	0.231	14.3(1.1)	14.0(1.2)	0.276
Gender							
Girls	67(50%)	30(49%)	37(51%)		---	---	---
Boys	67(50%)	31(51%)	36(49%)	0.862	---	---	---
PDE							
No	61(46%)	---	---	---	31(46%)	30(45%)	
Yes	73(54%)	---	---	---	36(54%)	37(55%)	0.863
Overall drug experimentation							
No drug experimentation	67(50%)	33(54%)	34(47%)		34(51%)	33(49%)	
At least one drug	67(50%)	28(46%)	39(53%)	0.386	33(49%)	34(51%)	0.863
Subtype drug experimentation							
No drug experimentation	67(50%)	33(54%)	34(47%)		34(51%)	33(49%)	
Tobacco and/or alcohol only	25(19%)	6(10%)	19(26%)	0.035†	12(18%)	13(19%)	0.815†
Marijuana/illegal drug	42(31%)	22(36%)	20(27%)	0.751†	21(31%)	21(31%)	0.940†
Externalizing score (mean, SD)	155.1(26.4)	153.6(30.4)	156.3(22.5)	0.564	153.6(30.4)	156.5(21.8)	0.529
Internalizing score (mean, SD)	359.9(58.8)	345.6(58.8)	371.9(56.4)	0.010	358.7(56.1)	360.9(61.7)	0.832
Perceived peer drug use							
No	40(30%)	18(30%)	22(30%)		17(25%)	23(34%)	
Yes	94(70%)	43(70%)	51(70%)	0.937	50(75%)	44(66%)	0.257
Current caregiver drug use							
No	117 (90%)	58(95%)	59(86%)		57(89%)	60(91%)	
Yes	13(10%)	3(5%)	10(14%)	0.084	7(11%)	6(9%)	0.777
Prenatal tobacco exposure (PTE)							
No	64(48%)	48(79%)	16(22%)		33(49%)	31(46%)	
Yes	70(52%)	13(21%)	57(78%)	<0.001	34(51%)	36(54%)	0.729
Prenatal alcohol exposure (PAE)							
No	84(63%)	50(82%)	34(47%)		42(63%)	42(63%)	

	Total	NE * (n=61, 46%)	PDE** (n=73, 54%)	p ***	Girls (n=67, 50%)	Boys (n=67, 50%)	P***
Yes	50(37%)	11(18%)	39(53%)	<0.001	25(37%)	25(37%)	1.000

* NE: prenatally drug non-exposed adolescents

** PDE: prenatal heroin/cocaine exposed adolescents

*** p values were based on T-test, chi-square or exact test, whichever is appropriate

† The p value is 0.035 for 2×2 crosstab between tobacco/alcohol only experimentation (vs. no experimentation of any drug) and PDE, 0.751 for the 2×2 crosstab between marijuana/illegal drug experimentation (vs. no experimentation of any drug) and PDE; 0.815 for the 2×2 crosstab between tobacco/alcohol only experimentation (vs. no experimentation of any drug) and gender, 0.940 for the 2×2 crosstab between marijuana/illegal drug experimentation (vs. no experimentation of any drug) and gender.

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Table 3

Odds Ratio of drug experimentation (experimentation with at least one drug) by adolescence in relation to prenatal heroin/cocaine exposure (PDE), behavioral problems and other sample characteristics (n=134).

	Abstainers (n=67, 50%)	Experimenters (n=67, 50%)	P*	Crude models		Model 1		Model 2	
				Crude OR**	p	aOR***	p	aOR	p
PDE									
No	33(54%)	28(46%)		1.00	ref.	1.00	ref	1.00	Ref
Yes	34(47%)	39(53%)	0.386	1.35(0.68–2.67)	0.386	0.78(0.27–2.21)	0.632	1.02(0.37–2.80)	0.975
Externalizing score									
(mean, SD)	147.3(19.3)	162.8(30.2)	0.001	2.09(1.33–3.29)	0.001	---	---	2.28(1.33–3.91)	0.003
Internalizing score									
(mean, SD)	349.2(59.1)	370.0(57.1)	0.042	1.45(1.01–2.08)	0.045	1.47(0.96–2.27)	0.079	---	---
Gender									
Girls	34(51%)	33(49%)		1.00	ref.	1.00	ref	1.00	ref
Boys	33(49%)	34(51%)	0.863	1.06(0.54–2.09)	0.863	1.25(0.58–2.73)	0.571	1.03(0.46–2.32)	0.943
Age	13.9(1.1)	14.4(1.2)	0.022	1.42(1.05–1.92)	0.024	1.43(1.02–2.02)	0.040	1.43(1.00–2.06)	0.051
Perceived peer drug use									
No	29(72%)	11(28%)		1.00	ref.	1.00	ref	1.00	ref
Yes	38(40%)	56(60%)	0.001	3.89(1.73–8.71)	0.001	4.36(1.78–10.65)	0.001	4.25(1.68–10.80)	0.002
Current caregiver drug use									
No	61(52%)	56(48%)		1.00	ref.	1.00	ref	1.00	ref
Yes	3(23%)	10(77%)	0.077	1.29(0.95–13.87)	0.059	2.81(0.69–10.65)	0.151	2.05(0.47–8.90)	0.336
Prenatal tobacco exposure (PTE)									
No	36(56%)	28(44%)		1.00	ref.	1.00	ref	1.00	Ref
Yes	31(44%)	39(56%)	0.166	1.62(0.82–3.20)	0.168	2.17(0.79–5.97)	0.135	2.09(0.75–5.81)	0.159
Prenatal alcohol exposure (PAE)									
No	43(51%)	41(49%)		1.00	ref.	1.00	ref	1.00	Ref
Yes	24(48%)	26(52%)	0.721	1.14(0.56–2.29)	0.721	0.66(0.27–1.60)	0.353	0.59(0.24–1.46)	0.252

* P values are based on T-tests, Chi-square tests or fisher exact tests, whichever are appropriate.

** Crude OR: crude Odds Ratio without adjusting for any other covariates.

*** aOR: adjusted Odds Ratio after adjusting for other variables in the same column; ORs or aORs for internalizing or externalizing problems refers to Odds Ratio of drug experimentation related to 1 SD change in the scores.

Table 4

Odds Ratio of subtype drug experimentation (experimentation with tobacco or alcohol only, and experimentation with marijuana and other illegal drugs, separately) in relation to prenatal heroin/cocaine exposure (PDE), behavioral problems and gender based on two separate logistic regression models.

	Experimentation with tobacco and/or alcohol only* (n=92)						Experimentation with marijuana and/or other illegal drugs* (n=109)					
	Crude models		Model 1		Model 2		Crude models		Model 1		Model 2	
	OR	p	aOR**	p	aOR**	p	OR	p	aOR**	p	aOR**	p
PDE	3.07(1.09–8.66)	0.034	0.97(0.26–3.67)	0.967	1.16(0.31–4.33)	0.831	0.88(0.41–1.91)	0.751	0.74(0.23–2.42)	0.617	1.02(0.33–3.10)	0.976
Externalizing problems	2.00(1.08–3.71)	0.027			2.38(1.05–5.37)	0.037	2.20(1.32–3.67)	0.002			2.65(1.40–5.02)	0.003
Internalizing problems	1.62(0.99–2.64)	0.054	1.82(0.97–3.41)	0.060			1.32(0.90–1.94)	0.152	1.38(0.89–2.19)	0.165		
Gender (boys vs. girls)	1.12(0.45–2.80)	0.815	1.33(0.43–4.15)	0.621	1.44(0.45–4.62)	0.540	1.03(0.48–2.23)	0.940	1.26(0.52–3.07)	0.611	1.07(0.41–2.76)	0.894

*Experimentation with subtype drug experimentation was compared to abstinence from using any drug.

**aOR: Odds Ratio of drug experimentation after adjusting for other variables in same column as well as age, perceived peer drug use, current caregiver drug use, prenatal tobacco exposure, and prenatal alcohol exposure. aORs for internalizing or externalizing problems refers to Odds Ratio related to 1 SD increase in the scores.

Table 5

Odds Ratios of drug experimentation in relation to internalizing problems, stratified by gender.

	Experimentation with at least one drug (n=134)				Experimentation with tobacco and/or alcohol only** (n=92)				Experimentation with marijuana and/or other illegal drugs** (n=109)			
	Boys		Girls		Boys		Girls		Boys		Girls	
	aOR*	p	aOR*	p	aOR*	p	aOR*	p	aOR*	p	aOR*	p
Internalizing problems	0.91(0.51–1.60)	0.734	2.82(1.34–5.94)	0.006	0.59(0.22–1.61)	0.301	3.88(1.30–11.53)	0.015	0.99(0.53–1.81)	0.943	2.00(0.93–4.30)	0.078

*aOR: Odds Ratio in relation to 1 SD change in internalizing problems for males or females, after adjusting for prenatal exposure to heroin/cocaine (PDE), age, perceived peer drug use, current caregiver drug use, prenatal tobacco exposure, and prenatal alcohol exposure.

**Experimentation with subtype drug experimentation was compared to abstinence from using any drug.