Published in final edited form as:

J Abnorm Child Psychol. 2016 April ; 44(3): 547–560. doi:10.1007/s10802-015-0052-5.

Psychological Distress Among School-Aged Children with and Without Intrauterine Cocaine Exposure: Perinatal Versus Contextual Effects

Mark A. Richardson^{1,2}, Wanda Grant-Knight³, Marjorie Beeghly^{4,5}, Ruth Rose-Jacobs^{6,7}, Clara A. Chen⁸, Danielle P. Appugliese⁸, Howard J. Cabral⁹, Jane M. Liebschutz¹⁰, and Deborah A. Frank^{6,7}

¹Division of Psychiatry, Boston University School of Medicine, Boston, MA, USA

²Department of Psychological and Brain Sciences, Boston University, 648 Beacon Street, 2nd floor, Boston, MA 02215, USA

³Private Practice, Wheaton, IL, USA

⁴Department of Psychology, Wayne State University, Detroit, MI, USA

⁵Division of Developmental Medicine, Boston Children's Hospital, Boston, MA, USA

⁶Division of Developmental and Behavioral Medicine, Boston Medical Center, Boston, MA, USA

⁷Department of Pediatrics, Boston University School of Medicine, Boston, MA, USA

⁸Data Coordinating Center, Boston University School of Public Health, Boston, MA, USA

⁹Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA

¹⁰General Internal Medicine, Department of Medicine, Boston Medical Center, Boston, MA, USA

Abstract

Whether intrauterine cocaine exposure (IUCE) explains unique variance in psychiatric functioning among school age children, even after controlling for other biological and social risk factors, has not been fully delineated. As part of a longitudinal birth cohort study of children with and without IUCE, we conducted and analyzed data based on structured clinical interviews with 105 children (57 % male) and their caregivers when the child was approximately 8.5 years old; 47 % of the children had experienced IUCE. Interviews included past and current major psychological disorders and sub-threshold mental health symptoms. Potential covariates were ascertained by interviews of birth mothers and other caregivers from shortly after the child's birth until the 8.5-year visit. More than one-third of children met DSM-IV criteria for one or more mood, anxiety, attention deficit, or disruptive behavior disorders. IUCE was not significantly associated with children's history of psychological distress, in either bivariate or multiple logistic regressions. In contrast, birth mothers' acknowledgement of greater psychiatric distress at baseline and higher levels of alcohol consumption during pregnancy, and at 8.5 years caregivers' reports of their own

Mark A. Richardson markrich@bu.edu.

Conflict of Interest Study authors declare that they have no conflict of interest.

psychological distress, and children's lower IQ were predictors of higher rates of psychological morbidity. Findings are consistent with prior reports suggesting that, regardless of IUCE status, children from low-income, urban backgrounds are at heightened risk for psychological distress. Results underscore the need for closer monitoring of the mental health of children living in low-income households, with or without intrauterine substance exposures, to facilitate access to appropriate services.

Keywords

Children; Intrauterine cocaine exposure; Caregiver psychiatric history; Intrauterine alcohol exposure

During the past two decades, multiple studies investigated whether, and under what conditions, intrauterine cocaine exposure (IUCE) predicts adverse outcomes in a variety of domains (Ackerman et al. 2010; Bada et al. 2007; Delaney-Black et al. 1998; Frank et al. 2001). A growing body of evidence suggests that IUCE is associated with poorer emotional regulation in preschool- and school-aged children (Bennett et al. 2008; Molitor et al. 2003). Such emotional dysregulation in childhood, particularly in the context of poverty and other environmental stressors, might presage an increased risk of mood and behavioral disorders both concurrently and in later life (Bennett et al. 2002; Kovacs et al. 2008).

Mayes (1999, 2002) described a theoretical model of the impact of IUCE on human arousal regulatory systems, suggesting that alterations in prefrontal cortex functions may contribute to early arousal regulation difficulties that might heighten children's later risk for developing anxiety and conduct disorders. Consistent with this model, several empirical studies of infants and toddlers indicate that IUCE is associated with alterations in emotional reactivity and expressivity during stressful situations (Beeghly et al. 2003; Bendersky and Lewis 1998; Bennett et al. 2002; Roumell et al. 1997). However, findings from the few studies that have evaluated whether IUCE is independently associated with the emergence of diagnosable psychological problems in children during the elementary school years are inconsistent and vary by investigative team.

Several investigators have examined the effects of prenatal exposure to cocaine and other substances on risk for challenging behaviors among school-aged children using dimensional rating procedures, with mixed results. After controlling for appropriate environmental factors, IUCE did not independently predict challenging behaviors as assessed using caregiver ratings on the Child Behavior Checklist (CBCL) (Achenbach 1991) in a diverse set of studies (Accornero et al. 2006; Kilbride et al. 2006; Richardson et al. 1996). In contrast, at least one study employing caregiver ratings (Bailey et al. 2005), one employing blinded examiner ratings of behavioral regulation problems (Accornero et al. 2011), and several employing blinded teacher ratings of challenging behavior reported either adverse independent effects of IUCE or effects that were mediated by gender and prenatal exposure to alcohol (Bailey et al. 2005; Delaney-Black et al. 2000, 2004).

However, relatively little is known about whether children prenatally exposed to cocaine manifest a heightened rate of clinically significant behavioral problems. In a prospective

study by Linares et al. (2006) which used a cartoon based self-report measure, 6-year-olds with IUCE were marginally more likely than same-aged children without IUCE to report symptoms in the probable clinical range for oppositional defiant disorder (ODD) and attention deficit hyperactivity disorder (ADHD), but not for other disorders. Similarly, Morrow et al. (2009) identified IUCE as a modest but statistically significant predictor of ADHD and ODD among 5-year old children who completed structured diagnostic interviews. In contrast, another article from the same longitudinal study reported that IUCE did not represent a statistically significant predictor of behavioral problems among children at age seven when caregivers, rather than children, provided information about psychological distress or dysfunction (Accornero et al. 2006).

Taken as a whole, research evidence to date does not consistently indicate clinically meaningful or statistically significant effects of IUCE on psychological functioning in childhood (Frank et al. 2001; Lambert and Bauer 2012). Given these limited and apparently inconsistent findings, further investigation of the influence of IUCE on clinical psychopathology among school-aged children appears to be sorely needed.

IUCE rarely occurs in isolation; mothers who use cocaine during pregnancy are also more likely to use substances other than cocaine (e.g., alcohol, tobacco, and marijuana) (Day and Richardson 1994; Moe and Slinning 2002). Prior studies indicate that prenatal exposure to alcohol, tobacco, and marijuana are independently associated with a variety of sub-optimal child outcomes (Bada et al. 2007; Day et al. 2000; Flak et al. 2014; Richardson et al. 2002; Tiesler and Heinrich 2014). Thus, there may be risks associated with the pharmacologic properties of specific substances to which children are exposed in utero, and others that are more generic to parents' substance use and/or associated environmental or genetic risks.

IUCE also may be a marker for a variety of contextual genetic and environmental predictors of psychopathology in school age children, including conditions such as parental psychopathology, substance misuse, maladaptive family dynamics, and exposure to violence. For example, even in the absence of substance use disorders, maternal psychopathology may heighten children's risk for psychological morbidity via genetic transmission, parenting factors, or gene-environment transactions (Spence et al. 2002; Sullivan et al. 2000). When coupled with problematic parental substance use, maternal psychopathology further compounds children's risk of maladaptation (Hans 2002; Minnes et al. 2010; Singer et al. 2002). In a large longitudinal study of at-risk families, Thompson et al. (2005) found that a history of maltreatment and violence exposure was associated with heightened psychological distress and greater suicidal ideation among 8-year-olds. Other studies identified significant associations between exposure to violence and symptoms of post-traumatic stress (Bailey et al. 2006), suicidal ideation (O'Leary et al. 2006) and depressive symptoms and aggression in girls (Forehand and Jones 2003).

Sex differences in adolescent and adult psychopathology are also well documented. However, research on childhood psychopathology does not always reflect consistent male/female differences (Shaffer et al. 2002), although some investigators report significant associations with the child's sex in select domains (Kovacs et al. 2003). This inconsistency also emerges in studies of IUCE. For example, a longitudinal prospective study found that,

when the sample was stratified by child's sex and prenatal alcohol exposure, girls with IUCE (but not prenatal alcohol exposure) were more aggressive than girls with both prenatal exposures, whether assessed via caregiver report (Sood et al. 2005) or teacher report (Bailey et al. 2005). In contrast, among boys, the combination of prenatal cocaine and alcohol exposures predicted more externalizing behavior problems (Bailey et al. 2005).

The primary aim of the present study was to examine whether IUCE is associated with school age children's display of psychiatric symptoms or diagnoses after controlling for prenatal exposures to other substances (marijuana, alcohol, tobacco) and selected biological and social factors known in other contexts to influence children's psychiatric symptoms and diagnoses. The current study is unique because it considers both caregiver and child reports in determining the presence of psychological morbidity, and ascertains formal diagnoses regarding both internalizing and externalizing conditions. Three specific hypotheses were evaluated in covariate-controlled analyses: 1) IUCE is independently associated with increased risk for psychological morbidity among school age children; 2) caregiver psychological distress independently increases the risk for psychological morbidity among school age children; and 3) select environmental factors (including violence exposure) are independently associated with increased risk for psychological morbidity among school age children.

Method

Recruitment

As previously reported in articles based on this prospective longitudinal study (Frank et al. 1999; Tronick et al. 1996), infant-birth mother dyads were recruited on maternity units between October 1990 and March 1993. Selection criteria included the following: eligible mothers were: 1) at least 18 years old; 2) fluent in English (as many study measures planned for this cohort at older ages were standardized only for English-speaking populations); 3) HIV-negative; and, 4) without indication, by either self-report or bioassays, of having used during pregnancy illegal opiates, methadone, amphetamines, phencyclidine, barbiturates, or hallucinogens. Infant inclusion criteria included: 1) gestational age at delivery ≥ 36 weeks; 2) no neonatal intensive care; 3) no obvious major congenital malformations; and 4) no diagnosis of HIV or Fetal Alcohol Syndrome. Maternal and infant characteristics obtained from medical record review at intake were confirmed by maternal interviews, infant physical exams, and/or biological assays. Further details about characteristics for the original sample for this longitudinal study are found in Table 1; additional information about recruitment procedures are reported elsewhere (Frank et al. 1999; Tronick et al. 1996).

Human Subjects

The Institutional Review Board of Boston City Hospital (now Boston Medical Center), the site of this longitudinal study, reviewed and approved all participant recruitment and assessment procedures, in accordance with ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Birth mothers and adult caregivers provided written informed consent and beginning at the 8.5-year follow-up, children gave

their written assent for study participation. A federal Certificate of Confidentiality protected sensitive data provided by and about participants from subpoena.

Sample Characteristics and Retention

Two hundred fifty two mother-child dyads (139 with IUCE, 113 unexposed) consented to participate in the first wave of this longitudinal study at the time of the infant's birth, for whom a demographic overview is offered in Table 1. Thirty-eight mother-child dyads were lost to further follow-up within 6 months of the child's birth. One hundred forty five (71 %) of the remaining families were retained in the longitudinal sample and participated in the 8.5-year assessment. Findings revealed limited evidence of differential attrition by IUCE status or by other intrauterine exposures, demographic, maternal, caregiver, or child variables. Specifically, a larger percentage of children retained in the 8.5-year sample (90 % versus 81 %) were born to African American / Caribbean mothers, $\chi^2 (df=1)=4.31, p=0.04$, a smaller percentage of mothers from families retained in the 8.5-year sample (41 % versus 58 %) reported at baseline a recent history of problems with illicit drugs on the Addiction Severity Index (ASI, please see below), $\chi^2 (df=1)=5.06, p=0.02$, and a smaller percentage of mothers from families retained in the 8.5-year sample (27 % versus 39 %) reported a recent history of psychiatric problems on the ASI at baseline, $\chi^2 (df=1)=3.86, p=0.05$. These variables were included as covariates in all primary analyses to control for these differences.

Of the group retained in the 8.5-year sample, 105 (72 %) completed psychiatric diagnostic interviews, providing key psychiatric variables for these analyses. Birth mothers were primarily young, single, African American / Caribbean, and had completed fewer than 12 years of formal education (see Table 2). Birth mothers in the IUCE group were significantly older, less likely to be married, more likely to have experienced previous pregnancies, and reported higher levels of alcohol, marijuana, and tobacco use during pregnancy than birth mothers in the non-IUCE group. Children in the IUCE group had significantly lower birth weights, experienced a greater number of caregiver changes since birth, and were less likely to be in the custody of their birth mother at the time of the 8.5-year visit. Non-birth mother caregivers in the present sample included the children's birth father ($n=5$), aunt ($n=1$), grandmother ($n=11$), great-grandmother ($n=2$), unspecified other relatives ($n=3$), adoptive mother ($n=7$), foster mother ($n=1$), and "other" non-relatives ($n=1$).

Procedures and Materials

Classification of Exposure Status—Recruited mothers were identified as cocaine users or non-users during pregnancy based on both biologic assays of mothers' and infants' urine (either during prenatal care or at delivery) and infants' meconium and maternal interview obtained on the maternity unit. All dyads received at least one biologic assay. Initially, heavier cocaine exposure reflected maternal self-reported cocaine use during pregnancy or level of cocaine metabolites in infant meconium that fell in the top quartiles for the sample; all others with IUCE were identified as with lighter exposure (Frank et al. 1999; Tronick et al. 1996). However, preliminary analyses revealed that level of IUCE was not associated with dependent variables of interest. Therefore, a dichotomous IUCE variable (exposed versus unexposed) was used in all subsequent analyses.

Follow-up at 8.5 Years—The present study utilized measures collected at the 8.5-year visit. At this visit, a clinical psychologist trained in psychiatric assessment and masked to children's IUCE and background variables (WGK) conducted separate diagnostic interviews with children and caregivers. Masters- or bachelors-level research assistants masked to children's IUCE, background variables, and psychiatric status assessed children's intelligence, while other research assistants independently conducted interviews with caregivers that included demographic information, self-report measures of psychological distress, patterns of current substance use, and family functioning.

Predictors

Child's Violence Exposure—Children's self-reported exposure to violence was measured using the Violence Exposure Scale for Children, Revised (VEX-R) (Fox and Leavitt 1995). The VEX-R evaluates children's exposure to violence as either a victim or witness. Items range in severity from relatively mild (e.g., being yelled at, pushed, or spanked) to relatively severe (e.g., being threatened with a weapon, shot, or stabbed). In prior research, internal consistency reliability of the VEX-R ranged from 0.80 to 0.86 (Shahinfar et al. 2000) and VEX-R scores were associated with children's level of emotional distress (Raviv et al. 1999). In the present study, data were visually inspected to determine the number of children reporting victimization versus witnessing violence; the percentage acknowledging victimization was too small to analyze separately. As such, the variable of interest for the present analyses differentiated those whose total VEX-R scores fell in the upper quartile of the distribution for all respondents in the present sample from those whose total VEX-R score fell below the upper quartile of this distribution. It is noteworthy that for ethical reasons and at the recommendation of pediatricians affiliated with this research team, a few children with the highest levels of clinically observed post-traumatic symptoms were not asked to complete this questionnaire.

Current Caregiver Distress—The Brief Symptom Inventory (BSI) (Derogatis 1993) is a 53-item-self-report instrument. The BSI is a short alternative to the complete Symptom Checklist-90-Revised (Derogatis 1977), designed to assess psychological symptoms during respondents' previous 7 days. The BSI assesses nine primary symptom dimensions and three global indices of distress; the present study employed the Global Severity Index (GSI), a measure the current overall caregiver psychological distress. Widely used in research with samples of substance-abusing women (e.g., Kettinger et al. 2000), the GSI has demonstrated very good reliability, with stability estimates approaching 0.90 (Derogatis 1993). Higher GSI scores reflect greater psychological distress.

Addiction Severity Index—The Addiction Severity Index (ASI) (McLellan et al. 1992), a semi-structured interview, assessed seven potential problem areas in individuals with substance use histories: medical status, employment and financial support, drug use, alcohol use, legal status, family/social status, and psychiatric status. Information from the ASI administered to birth mothers at the time of the infant's birth and to current primary caregivers (72 % of whom were birth mothers) at the 8.5-year visit was used to assess caregivers' problems within these domains over the previous 30-day period. The ASI has been widely used with samples of substance-using women with demographics

characteristics similar to those of the current sample (Brown et al. 1993) and demonstrated good to excellent reliability for composite index scores for wide-ranging samples (Zanis et al. 1997). Higher ASI composite scores reflect more problematic functioning.

Outcomes

Diagnostic Interview—At the 8.5-year visit, children's psychiatric functioning was evaluated using the child and parent versions of the Diagnostic Interview for Children and Adolescents (DICA) (Reich 2000), a structured interview using Diagnostic and Statistical Manual-Fourth Edition (DSM-IV; American Psychiatric Association 1994) criteria to explore the presence of symptoms and diagnoses of psychological disorders. The DICA is widely used to assess psychiatric morbidity in children and adolescents and has demonstrated good reliability in young respondents (Reich 2000). At the time this phase of the research was initially proposed, the investigative team based its selection of appropriate diagnostic instrumentation and modules on a number of factors, including prior literature on the development, expression, and prevalence of psychological disorders in children (e.g., Kazdin and Kagan 1994), as well as literature regarding the potential for adverse influences of IUCE on behavioral health development (e.g., Scherling 1994). In addition, the selection of diagnostic instruments reflects the research team's collective experience working with this sample, and the team's experience working with children at the urban medical center that served as the base for this longitudinal study. DICA modules administered to children included: Post-Traumatic Stress Disorder (PTSD); Depression; Separation Anxiety Disorder; and Generalized Anxiety Disorder. Independent caregiver interviews about children's functioning utilized the PTSD, Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder, and Conduct Disorder modules. Child and caregiver modules were divided in this way because research evidence suggests that school-aged children are better reporters of their internalizing symptoms than are their caregivers or other adults in their environment, whereas caregivers and others are typically better reporters of children's externalizing behaviors (Cantwell et al. 1997). DICA symptoms were coded as endorsed only if diagnostic scoring criteria, including presence of impairment, were unequivocal. In the rare event that a child became distressed during the interview or reported issues of concern (such as current abuse), the child psychologist conducting these interviews used clinical discretion in deciding whether the interview should be abbreviated or terminated. Appropriate recommendations for further intervention (e.g., referral for urgent behavioral health evaluation or outpatient therapy) were made on the rare occasions when interviews were prematurely terminated because of distress.

Scoring of the DICA modules yielded two sets of summary dependent variables reflecting lifetime psychiatric morbidity: (1) number of: a) any diagnoses; b) internalizing disorder diagnoses; and c) externalizing disorder diagnoses; and, (2) number of: a) any major psychiatric symptoms; b) symptoms of internalizing disorder; and c) symptoms of externalizing disorder. Internalizing and externalizing symptom classifications were determined by summing the symptoms for diagnoses falling into either the internalizing or externalizing categories. This method of categorizing symptoms and diagnoses has been used previously to analyze DICA psychiatric outcomes (e.g., Ezpeleta et al. 2011). Symptom

counts help account for potentially relevant psychiatric outcomes that do not reach diagnostic criteria for major psychiatric syndromes.

We created composite internalizing symptom / diagnosis scores by tallying symptoms and formal diagnoses of depression, separation anxiety disorder, generalized anxiety disorder, and PTSD. Externalizing symptom / diagnosis scores account for indicators of ADHD, conduct disorder, and oppositional defiant disorder. Because PTSD was the only module administered to both caregivers and children, symptom reports were combined such that items endorsed by both caregiver and child were counted as one symptom, and items endorsed by either increased the count by one, insuring the inclusion of symptoms reported by either party in the PTSD count.

Covariates

The pool of covariates evaluated for possible inclusion in the multivariate models included prenatal substance exposures other than cocaine, birth mothers' characteristics at baseline and at the 6-month follow-up visit, children's characteristics at birth and at the 8.5-year follow-up visit, and primary care-givers' characteristics (and of the families with whom children resided) at the 8.5-year follow-up visit. Specifically, potential covariates for intrauterine substance exposures other than cocaine included: alcohol (self-reported daily average number of alcoholic drinks consumed during the 30 days prior to birth [log transformed]); tobacco (self-reported daily average number of cigarettes mother smoked during pregnancy); and marijuana (any self-reported marijuana use during pregnancy or positive urine or meconium assay for cannabinoids). Potential covariates for birth mothers included: age at the time of the child's birth; marital status; parity; and composite scores for the ASI Psychological Problems, Drugs, and Alcohol scales. Birth mother's total score from the Center for Epidemiological Studies-Depression scale (CES-D; Radloff 1977) was measured at 6 months postpartum. Potential covariates based on evaluation of children included: birth weight; sex; current custody arrangements (biological mother, kinship caregiver, or non-kin foster caregiver, ascertained regularly from the 6-month through the 8.5-year visit to sum number of caregiver changes), as well as a variety of measures ascertained at the time of the DICA assessment, including age and prorated Full Scale IQ on the Wechsler Intelligence Scales for Children-Third Edition (WISC-III; Wechsler 1991). Potential covariates obtained from current caregivers at the time of the DICA assessment included: average daily consumption of alcohol during the preceding 30 day period; average number of cigarettes smoked during the preceding 30 day period; any marijuana use during the preceding 30 day period; composite scores for the ASI Psychological Problem, Drugs, and Alcohol scales; family conflict (Conflict Resolution Scale total score (Straus 1974); and incarceration of parent or primary caregiver at any time during the previous 24 months. The specific covariates retained in different multivariate models varied, dependent on their association with the dependent variable in question.

Statistical Analyses

Data Imputation—Data was missing for select predictors or covariates. IQ scores from assessments close to the target timeframe were used in place of missing prorated IQ values at the 8.5-year follow-up. Missing values among the other covariates were multiply imputed

using monotone methods (SAS PROC MI) based on non-missing data from similar variables at adjacent assessments, generating 10 data sets. VEX-R scores that were missing due to clinician concern were imputed with an additional flag to indicate greater likelihood of being in the highest quartile. Each data set was analyzed in the multivariate models, and results were combined across data sets using PROC MIANALYZE.

Bivariate Analyses—Association between IUCE and children's diagnostic status variables were evaluated using chi square analyses. Associations between IUCE and symptom counts were evaluated using *t*-tests.

Selection of Covariates—A list of possible covariates was selected on theoretical grounds at the onset of the study and examined in relation to IUCE and children's psychiatric outcomes. To maximize the ability to identify IUCE effects, only variables that were significantly associated with IUCE and/or with a specific outcome at the $p=0.10$ level in bivariate analyses were also included in multivariate regression models described below.

Multivariate Regression—Separate poisson regression analyses were used to evaluate the association between IUCE and symptom counts or lifetime diagnosis counts for each composite diagnostic category (total, externalizing, and internalizing), controlling for relevant covariates. Poisson regression takes into account the relatively high rate of participants with DICA symptom or diagnosis counts of zero; the over dispersion of null diagnostic findings is adjusted for using the scaled deviance method (Stokes et al. 2000).

All potential covariates were included in the first model for each dependent variable of interest. In the second model, we retained all covariates associated with the dependent or independent variables at or below the $p=0.10$ level. In subsequent models, covariates no longer associated with the dependent variable at or below the $p=0.10$ level were removed, until all retained covariates were associated at or below the $p=0.10$ level with the dependent variable in question.

Results for all analyses were deemed statistically significant when the *p*-value was less than or equal to 0.05 for two-tailed tests of significance. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, North Carolina).

Results

Study Sample

The only significant difference between participants in the 105 dyads who completed diagnostic interviews and among the 40 who did not was that the percentage of girls among those completing diagnostic interviews (43 %) was smaller than the percentage of girls among who did not complete these interviews (63 %), $\chi^2 (df=1)=4.48, p=0.04$. Reasons for not completing diagnostic assessment included scheduling conflicts with the clinician available for to complete child diagnostic interviews ($n=20$), family time constraints ($n=5$), failure of the child to complete the 8.5-year neurodevelopmental assessments ($n=7$), or unknown ($n=8$).

There were no significant differences between the 105 children who completed DICA interviews and the 40 who did not on caregivers' concurrent report of children's total behavior problems on the CBCL, or estimated general cognitive abilities (WISC-III). This suggests that the children retained in the present sample were neither more nor less likely than non-participants to have identifiable cognitive or behavioral difficulties.

The present sample also did not differ significantly by IUCE status on mothers' level of self-reported depressive symptoms on the CES-D at the 6-month interview. Moreover, the current sample did not differ by IUCE status in caregivers' level of psychiatric distress as measured by the ASI or BSI, current substance use, perceptions of family conflict as measured by the Conflict Resolution Scale or in the presence/absence of parent/caregiver incarceration in the previous 24 months.

Bivariate Associations Between IUCE and children's Psychiatric Functioning

Descriptive statistics regarding children's DICA diagnostic status and symptom counts by IUCE classification are in Table 3. The most frequently observed diagnoses were Oppositional Defiant Disorder, PTSD, and ADHD. However, *t*-tests revealed no significant IUCE group differences for the number of children's lifetime diagnoses (total diagnoses, internalizing diagnoses, and externalizing diagnoses), individual diagnostic categories, or symptom counts (total symptoms, internalizing symptoms, and externalizing symptoms).

Bivariate Association Between Covariates and Psychiatric Outcomes

Outcome measures were associated ($p < 0.10$) with: prenatal exposure to alcohol (total and internal diagnosis counts, internal symptom counts), tobacco (total and external diagnosis counts), and marijuana (total and internal diagnosis, external symptom counts); birth mothers' age (external symptom counts); marital status (total symptom counts); parity (external diagnosis counts); ASI illicit substance, alcohol (total and external diagnosis counts, total and external symptom counts), legal (total symptom counts), medical (internal symptom counts), and psychiatric (external symptom counts) composite scores during the perinatal period. At the 8.5-year assessment these outcomes correlated with: caregiver's psychological distress (BSI) (total and external symptom counts); children's age (external diagnosis counts) and IQ (external diagnosis and external symptom counts); violence exposure (highest quartile, VEX-R) (total symptom counts); modified Conflict Resolution Strategy score (external diagnosis and total and external symptom counts); and caretaker's ASI family/social (external diagnosis counts) and psychiatric (total and external diagnosis, and total, internal, and external symptom counts) composite scores; caregiver cigarette smoking (total and external diagnosis, total and external symptom counts); and whether any parent was incarcerated in the past 2 years (total and external diagnosis, external symptom counts).

Multivariate Poisson Regression Results for Symptom Counts

Results of multivariate Poisson regressions for lifetime symptom counts (see Table 4) indicated that IUCE was not associated with increased risk of psychiatric symptomatology as assessed via the DICA. Rather, factors identified as significant predictors of symptom counts were consistent with those identified as significant predictors of lifetime diagnosis

counts. In the final models predicting total symptom counts, only caregivers' ASI psychiatric composite score at the 8.5-year follow-up positively predicted total symptom counts. Total externalizing symptom counts were significantly predicted by caregivers' ASI psychiatric composite score at the 8.5-year follow-up, and birth mothers' ASI psychiatric composite score during the perinatal period. In addition, birth mothers' ASI alcohol composite scores during the postpartum period, and the child's prorated IQ at the 8.5-year visit were significantly and inversely predictive of externalizing symptom counts. Finally, birth mothers' higher average daily alcohol consumption (log transformation) during the 30-day period immediately preceding delivery and caretakers' ASI psychiatric composite score at the 8.5-year visit of recent psychological difficulty emerged as significant predictors of internalizing symptom counts. Further analyses examining the effects of the interaction between IUCE and level of alcohol exposure, and the interaction between IUCE and child sex were not statistically significant for any symptom count measure.

Multivariate Poisson Regression Results for Diagnosis Counts

Results of multivariate Poisson regressions for total lifetime diagnosis counts (see Table 4) indicated that IUCE was not a significant predictor of psychiatric morbidity. However, several other factors predicted psychiatric morbidity. In the final models predicting total diagnosis count, caregivers' ASI psychiatric composite score at the 8.5-year follow-up assessment positively predicted total diagnosis counts of the children, whereas birth mothers' ASI alcohol composite score during the perinatal period was inversely related to total diagnosis counts. A similar pattern was observed for the overall number of diagnoses for externalizing disorders, with caregivers' ASI psychiatric composite score at the 8.5-year follow-up positively predicting the child's total externalizing diagnosis counts. Similarly, birth mothers' ASI alcohol composite score during perinatal period and children's prorated IQ at the 8.5-year visit were inversely related to total externalizing diagnosis counts. In contrast, only one factor emerged as a significant positive predictor of internalizing diagnosis counts; birth mothers' average reported daily alcohol consumption (log transformation) during the 30-day period immediately preceding delivery. Further analyses examining the effects of the interaction between IUCE and level of alcohol exposure, and the interaction between IUCE and child sex were not statistically significant for any diagnosis count measure.

Discussion

This study extends previous investigations by examining the psychological functioning of school age children with and without IUCE in a low-income urban non-referred sample. The present study employed a standardized structured diagnostic interview and multiple informants to assess psychological distress, as well as evaluating other salient variables including, but not limited to, intrauterine exposure to other substances, exposure to violence, and earlier and concurrent psychological distress among birth mothers, and other guardians. In contrast to prior studies using behavioral rating scales (Accornero et al. 2006; Linares et al. 2006) or clinical interviews (Morrow et al. 2009), the present findings do not demonstrate a significant association between IUCE and elevated psychological distress among school-aged children. Rather, current findings indicate that contextual (family-based) factors

explain more of the variance in children's psychological distress than does their IUCE status. These apparently contrasting findings may reflect a variety of factors, including differences in experiences among respondents in these distinct studies, procedural differences (e.g., type of assessment techniques or informant utilized), age and cohort differences, and/or the range of cofactors included in primary analyses.

Current findings reflect that, regardless of IUCE status, the prevalence of psychological morbidity among children in the present sample was very high, with more than one-third of the sample meeting formal DSM IV criteria for diagnosis for one or more disorder. At first glance, this finding appears consistent with prior reports of heightened psychological distress among children born to mothers from low-income backgrounds without a known perinatal history of cocaine use (Costello et al. 2003; Kim-Cohen et al. 2003) and are higher than rates reported for a younger sample with otherwise similar risk indices (Morrow et al. 2009). However, recent literature on the rates of psychological disturbance in children and adolescents suggest lower prevalence estimates when both impairment criteria and symptom endorsement are considered in making diagnostic determination. In the current study, impairment was required to make a formal diagnosis using the DICA; therefore, for the present sample, the prevalence of psychological disorders was higher than might be expected, particularly considering that these children were younger than were the children in prior studies (Ezpeleta et al. 2001).

Although IUCE was not a significant predictor of psychopathology in the current sample, other biologic and social variables were associated with children's psychological functioning. Consistent with the work of others in cohorts established to study IUCE (Bennett et al. 2002; Hurt et al. 2001), current caregivers' report of their own psychological distress or need for treatment due to recent psychological distress was the variable most consistently associated with children's lifetime level of psychiatric symptoms and diagnostic status. This may suggest a non-specific but enhanced genetic and/or environmental vulnerability for psychological distress among these children. In contrast, the present findings may suggest that distressed caregivers tend to view their children's past or recent behavior in a more negative light than non-distressed caregivers, which may help explain this association for externalizing behavior, a finding consistent with a limited set of prior studies (e.g., Chi and Hinshaw 2002; Youngstrom et al. 1999). We should note that extant literature suggests that caregiver distress is more likely to bias perception of internalizing symptoms (Connell and Goodman 2002; Kroes et al. 2003).

Among other bivariate findings, level of maternal alcohol consumption during the month immediately prior to childbirth was associated with increased risk of internalizing symptoms and diagnoses, partially corroborating others' work (Hill et al. 2000; Rose-Jacobs et al. 2012; Walthall et al. 2008). In contrast, and contrary to our expectations, birth mothers' acknowledgement of problems associated with alcohol use and their need for alcohol-related treatment predicted a lower risk that their offspring would later evidence significant overall psychological distress, or signs of externalizing disorders. This association to our knowledge has not previously been identified among prenatally exposed children and suggests that mothers' acknowledgement of alcohol-related problems following delivery may lead to their greater efforts designed to protect children from distressing consequences.

Finally, children's prorated IQ was a modest, secondary (inverse) predictor of externalizing symptoms and diagnoses. Current results are consistent with prior findings of the association between these factors (e.g., Andersson and Sommerfelt 2001; Goodman et al. 1995), suggesting compromised generalized coping abilities among children with lower IQ scores.

Strengths and Limitations

To our knowledge, this longitudinal prospective study is the first to evaluate the association between IUCE and school-aged children's psychiatric functioning using a formal diagnostic interview (DICA) conducted with both parent and child, particularly in a low-income urban non-referred sample. Current findings need to be replicated in larger samples of low-income, urban children to evaluate their reliability. Replication might also allow for examination of whether specific biologic and environmental risk factors are associated with specific psychiatric diagnoses (such as ADHD and depression), as well as the global measures of lifetime psychiatric status evaluated in the present study. These global measures of externalizing and internalizing disorders may not be sufficiently sensitive to identify the particular type and context of distress exhibited by children with IUCE (Bennett et al. 2002).

A related limitation is that the current analyses are based on a demographically homogeneous sample of caregiver-child dyads from low-income, urban backgrounds. Thus, current findings may not generalize to other, more demographically diverse groups. Moreover, results need replication at older ages. In addition, self-report measures of substance use - - including cocaine use - - by birth mothers emphasized the period immediately preceding childbirth and the presence of metabolites in meconium (a cumulative indicator from about 20 weeks), rather than a review of substance use throughout pregnancy.

Although we did not find a significant association between IUCE and children's psychiatric functioning at 8.5 years of age in this sample, it is unclear whether IUCE will be associated with psychopathology later in life, including when children enter adolescence, and whether symptoms that might later arise in this sample will be of clinical significance. It is possible that as children mature, IUCE may be associated with children's diagnostic status, particularly because some important psychopathologies (including mood and substance-related disorders) do not emerge or reach their peak until adolescence.

Formal diagnostic evaluation of participating birth mothers and current caregivers was beyond the scope of the present study. As a result, there was no way to examine more directly the relationship between child and caregiver psychological symptoms or diagnoses. Current findings demonstrated a significant relationship between caregivers' current psychological distress and children's psychological functioning, introducing the possibility of caregiver bias that cannot be adequately disaggregated in this sample.

Despite these limitations, a primary finding of this study was that IUCE was not associated with children's history of psychological functioning by 8.5 years of age in this low-income, urban sample. Clinicians, educators, and researchers should thus be discouraged from accepting IUCE as a primary explanatory factor in the emergence of child psychopathology. Instead, professionals must seek to identify other factors influencing psychological

development, as well as to identify concurrent potentially modifiable environmental stressors that may help explain child psychosocial distress. The current study also suggests that these concurrent risk variables explain more of the variance in children's psychological distress than their IUCE status.

Moreover, although the clinical significance of distress associated with symptom counts in the current sample is not clear, the presence and relationship of these counts to established risk factors suggests that the evaluation of sub-threshold psychological syndromes warrants further investigation in future research among children and caregivers in high-risk samples. This appears particularly true given the high rates of endorsement of both psychiatric symptoms and syndromes in this non-referred urban sample. These findings indicate a need for clinicians to incorporate screening for psychopathology in low-income samples of school-aged children with wide-ranging environmental risks, regardless of history of intrauterine substance exposure. Such screening would help ensure that children experiencing psychological distress are promptly identified and monitored, whether or not these symptoms meet the threshold for clinically significant disorder, so that appropriate, timely interventions can be provided.

Acknowledgments

The authors are grateful to the families for their participation in this study. We also acknowledge research staff in the developmental lab at Boston Medical Center for their valuable assistance with data collection and reduction in this project.

The research presented in this paper was supported, in part, by a grant from the National Institute of Drug Abuse (R01DA6532) to Deborah A. Frank, PI, and by a grant from NIH/NCRR (M01RR00533).

All research was approved by the Institutional Review Board of the Boston Medical Center / Boston University School of Medicine and conducted with the informed consent of participating caregivers and assent of participating children.

References

- Accornero VH, Anthony JC, Morrow CE, Xue L, Bandstra ES. Prenatal cocaine exposure: an examination of childhood externalizing and internalizing behavior at age 7 years. *Epidemiologia e Psichiatria Sociale*. 2006; 15:20–29. [PubMed: 16584100]
- Accornero VH, Anthony JC, Morrow CE, Xue L, Mansoor E, Johnson AL, et al. Estimated effect of prenatal cocaine exposure on examiner-rated behavior at age 7 years. *Neurotoxicology and Teratology*. 2011; 33:370–378. doi:10.1016/j.ntt.2011.02.014. [PubMed: 21640292]
- Achenbach, TM. Manual for the child behavior checklist/4-18 and 1991 child profile. University of Vermont; Burlington: 1991.
- Ackerman JP, Riggins T, Black MM. A review of the effects of prenatal cocaine exposure among school-aged children. *Pediatrics*. 2010; 125:20–29. doi:10.1542/peds.2009-0637.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders: fourth edition (DSM-IV). American Psychiatric Association; Washington, D.C.: 1994.
- Andersson HE, Sommerfelt K. The relationship between cognitive abilities and maternal ratings of externalizing behaviors in preschool children. *Scandinavian Journal of Psychology*. 2001; 42:437–444. doi:10.1111/1467-9450.00256. [PubMed: 11771813]
- Bada HS, Das A, Bauer CR, Shankaran S, Lester B, LaGasse L, et al. Impact of prenatal cocaine exposure on child behavior problems through school age. *Pediatrics*. 2007; 119:e348–e359. doi: 10.1542/peds.2006-1404. [PubMed: 17272597]

- Bailey BN, Sood BG, Sokol RJ, Ager J, Janisse J, Hannigan JH, et al. Gender and alcohol moderate prenatal cocaine effects on teacher-report of child behavior. *Neurotoxicology and Teratology*. 2005; 27:181–189. doi:10.1016/j.ntt.2004.10.004. [PubMed: 15734269]
- Bailey BN, Hannigan JH, Delaney-Black V, Covington C, Sokol RJ. The role of maternal acceptance in the relation between community violence exposure and child functioning. *Journal of Abnormal Child Psychology*. 2006; 34:57–70. doi:10.1007/s10802-005-9002-y. [PubMed: 16468089]
- Beeghly M, Frank DA, Rose-Jacobs R, Cabral H, Tronick EZ. Level of prenatal cocaine exposure and infant-caregiver attachment behavior. *Neurotoxicology and Teratology*. 2003; 25:23–38. doi: 10.1016/S0892-0362(02)00323-9. [PubMed: 12633734]
- Bendersky M, Lewis M. Arousal modulation in cocaine-exposed infants. *Developmental Psychology*. 1998; 34:555–564. doi:10.1037/0012-1649.34.3.555. [PubMed: 9597364]
- Bennett DS, Bendersky M, Lewis M. Children's intellectual and emotional-behavioral adjustment at 4 years as a function of cocaine exposure, maternal characteristics, and environmental risk. *Developmental Psychology*. 2002; 38:648–658. doi:10.1037/0012-1649.38.5.648. [PubMed: 12220044]
- Bennett DS, Bendersky M, Lewis M. Children's cognitive ability from 4 to 9 years old as a function of prenatal cocaine exposure, environmental risk, and maternal verbal intelligence. *Developmental Psychology*. 2008; 44:919–928. doi:10.1037/0012-1649.44.4.919. [PubMed: 18605824]
- Brown LS, Alterman AI, Rutherford MJ, Cacciola JS, Zaballero AR. Addiction Severity Index scores of four racial/ethnic and gender groups of methadone maintenance patients. *Journal of Substance Abuse*. 1993; 5:269–279. doi:10.1016/0899-3289(93)90068-M. [PubMed: 8312732]
- Cantwell DP, Lewinsohn PM, Rohde P, Seeley JR. Correspondence between adolescent report and parent report of psychiatric diagnostic data. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:610–619. doi:10.1097/00004583-199705000-00011. [PubMed: 9136495]
- Chi TC, Hinshaw SP. Mother-child relationships of children with ADHD: the role of maternal depressive symptoms and depression-related distortions. *Journal of Abnormal Child Psychology*. 2002; 30:387–400. doi:10.1023/A:1015770025043. [PubMed: 12109489]
- Connell AM, Goodman SH. The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: a meta-analysis. *Psychological Bulletin*. 2002; 128:746–773. doi:10.1037/0033-2909.128.5.746. [PubMed: 12206193]
- Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry*. 2003; 60:837–844. doi: 10.1001/archpsyc.60.8.837. [PubMed: 12912767]
- Day NL, Richardson GA. Comparative teratogenicity of alcohol and other drugs. *Alcohol Health and Research World*. 1994; 18:42–48.
- Day NL, Richardson GA, Goldschmidt MD, Cornelius M. Effects of prenatal tobacco exposure on preschoolers' behavior. *Journal of Developmental and Behavioral Pediatrics*. 2000; 21:180–188. [PubMed: 10883878]
- Delaney-Black V, Covington C, Templin T, Ager J, Martier S, Sokol R. Teacher-assessed behavior of children prenatally exposed to cocaine. *Pediatrics*. 1998; 102:945–950. [PubMed: 9755270]
- Delaney-Black V, Covington C, Templin T, Ager J, Nordstrom-Klee V, Martier S, et al. Teacher-assessed behavior of children prenatally exposed to cocaine. *Pediatrics*. 2000; 106:782–791. doi: 10.1542/peds.2009-0637. [PubMed: 11015523]
- Delaney-Black V, Covington C, Nordstrom B, Ager J, Janisse J, Hannigan JH, et al. Prenatal cocaine: quantity of exposure and gender moderation. *Developmental and Behavioral Pediatrics*. 2004; 25:254–263.
- Derogatis, L. SCL-90-R. Manual-I. John Hopkins; Baltimore: 1977.
- Derogatis, L. BSI: Brief Symptom Inventory: Administration, scoring and procedures manual. 4th ed.. National Computer Systems; Minneapolis: 1993.
- Ezpeleta L, Keeler G, Erkanli A, Costello EJ, Angold A. Epidemiology of psychiatric disability in childhood and adolescence. *Journal of Child Psychology and Psychiatry*. 2001; 42:901–914. doi: 10.1111/1469-7610.00786. [PubMed: 11693585]

- Ezpeleta L, de la Osa N, Granero R, Doménech JM, Reich W. The diagnostic interview of children and adolescents for parents of preschool and young children: psychometric properties in the general population. *Psychiatric Research*. 2011; 190:137–144. doi:10.1016/j.psychres.2011.04.034.
- Flak AL, Su S, Denny CH, Kesmodel US, Cogswell ME. The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: a meta-analysis. *Alcoholism: Clinical and Experimental Research*. 2014; 38:214–226. doi:10.1111/acer.12214.
- Forehand R, Jones DJ. Neighborhood violence and coparent conflict: Interactive influence on children's psychosocial adjustment. *Journal of Abnormal Child Psychology*. 2003; 31:591–604. doi:10.1023/A:1026206122470. [PubMed: 14658740]
- Fox, NA.; Leavitt, LA. The violence exposure scale for children-VEX. University of Maryland; College Park: 1995.
- Frank DA, McCarten KM, Robson CD, Mirochnick M, Cabral H, Park H, Zuckerman B. Level of in utero cocaine exposure and neonatal ultrasound findings. *Pediatrics*. 1999; 104:1101–1105. [PubMed: 10545554]
- Frank DA, Augustyn M, Grant Knight W, Pell T, Zuckerman B. Growth, development, and behavior in early childhood following prenatal cocaine exposure: a systematic review. *Journal of the American Medical Association*. 2001; 285:1613–1625. doi:10.1001/jama.285.12.1613. [PubMed: 11268270]
- Goodman R, Simonoff E, Stevenson J. The impact of child IQ, parent IQ and sibling IQ on child behavioural deviance scores. *Journal of Child Psychology and Psychiatry*. 1995; 36:409–425. doi: 10.1111/j.1469-7610.1995.tb01299.x. [PubMed: 7782405]
- Hans SL. Studies of prenatal exposure to drugs: focusing on parental care of children. *Neurotoxicology and Teratology*. 2002; 24:329–337. doi:10.1016/S0892-0362(02)00195-2. [PubMed: 12009488]
- Hill SY, Lowers L, Locke-Welman J, Shen S. Maternal smoking and drinking during pregnancy and the risk for child and adolescent psychiatric disorders. *Journal of Studies on Alcohol*. 2000; 61:661–668. [PubMed: 11022804]
- Hurt H, Malmud E, Betancourt LM, Brodsky NL, Giannetta JM. A prospective comparison of developmental outcome of children with in utero cocaine exposure and controls using the Battelle Developmental Inventory. *Journal of Developmental and Behavioral Pediatrics*. 2001; 22:27–34. doi:10.1097/00004703-200102000-00005. [PubMed: 11265920]
- Kazdin AE, Kagan J. Models of dysfunction in developmental psychopathology. *Clinical Psychology: Science and Practice*. 1994; 1:35–52. doi:10.1111/j.1468-2850.1994.tb00005.x.
- Kettinger LA, Nair P, Schuler ME. Exposure to environmental risk factors and parenting attitudes among substance-abusing women. *American Journal on Drug and Alcohol Abuse*. 2000; 26:1–11. doi:10.1038/jp.2012.90.
- Kilbride HW, Castor CA, Fuger KL. School-age outcome of children with prenatal cocaine exposure following early case management. *Journal of Developmental and Behavioral Pediatrics*. 2006; 27:181–187. doi:10.1097/00004703-200606000-00001. [PubMed: 16775513]
- Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R. Prior juvenile diagnoses in adults with mental disorder. *Archives of General Psychiatry*. 2003; 60:709–717. doi:10.1001/archpsyc.60.7.709. [PubMed: 12860775]
- Kovacs M, Obrosky DS, Sherril J. Developmental changes in the phenomenology of depression in girls compared to boys from childhood onward. *Journal of Affective Disorders*. 2003; 74:33–48. doi: 10.1016/S0165-0327(02)00429-9. [PubMed: 12646297]
- Kovacs M, Joormann J, Gotlib IH. Emotion (dys)regulation and links to depressive disorders. *Child Development Perspectives*. 2008; 2:149–155. doi:10.1111/j.1750-8606.2008.00057.x. [PubMed: 20721304]
- Kroes G, Veerman JW, De Bruyn EEJ. Bias in parental reports? Maternal psychopathology and the reporting of problem in clinic-referred children. *European Journal of Psychological Assessment*. 2003; 3:195–203. doi:10.1027//1015-5759.19.3.195.
- Lambert BL, Bauer CR. Developmental and behavioral consequences of prenatal cocaine exposure: a review. *Journal of Perinatology*. 2012; 32:819–828. doi:10.1038/jp.2012.90. [PubMed: 22791278]
- Linares TJ, Singer LT, Kirchner L, Short EJ, Min MO, Hussey P, Minnes S. Mental health outcomes of cocaine-exposed children at 6 years of age. *Journal of Pediatric Psychology*. 2006; 31:85–87. doi: 10.1093/jpepsy/jsj020. [PubMed: 15802608]

- Mayes LC. Developing brain and in utero cocaine exposure: effects on neural ontogeny. *Development and Psychopathology*. 1999; 11:685–714. doi:10.1017/S0954579499002278. [PubMed: 10624721]
- Mayes LC. A behavioral teratogenic model of the impact of prenatal cocaine exposure on arousal regulatory systems. *Neurotoxicology and Teratology*. 2002; 24:385–395. doi:10.1016/S0892-0362(02)00200-3. [PubMed: 12009493]
- McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, et al. The fifth edition of the addiction severity index. *Journal of Substance Abuse Treatment*. 1992; 9:199–213. doi:10.1016/0740-5472(92)90062-S. [PubMed: 1334156]
- Minnes S, Singer LT, Kirchner HL, Short E, Lewis B, Satayathum S, Queh D. The effects of prenatal cocaine exposure on problem behavior in children 4–10 years. *Neurotoxicology and Teratology*. 2010; 32:443–451. doi:10.1016/j.ntt.2010.03.005. [PubMed: 20227491]
- Moe V, Slinning K. Prenatal drug exposure and the conceptualization of long-term effects. *Scandinavian Journal of Psychology*. 2002; 43:41–47. doi:10.1111/1467-9450.00267. [PubMed: 11885759]
- Molitor A, Mayes LC, Ward A. Emotion regulation behavior during a separation procedure in 18-month-old children of mothers using cocaine and other drugs. *Development and Psychopathology*. 2003; 15:39–54. doi:10.1017/S0954579403000038. [PubMed: 12848434]
- Morrow CE, Accornero VH, Xue L, Manjunath S, Culbertson JL, Anthony JC, Bandstra ES. Estimated risk of developing selected DSM-IV disorders among 5-year-old children with prenatal cocaine exposure. *Journal of Child and Family Studies*. 2009; 18:356–364. doi:10.1007/s10826-008-9238-6.
- O'Leary CC, Frank DA, Grant-Knight W, Beeghly M, Augustyn M, Rose-Jacobs R, et al. Suicidal ideation among urban nine and ten year olds. *Journal of Developmental and Behavioral Pediatrics*. 2006; 27:33–39. doi:10.1097/00004703-200602000-00005. [PubMed: 16511366]
- Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1:385–401. doi:10.1177/014662167700100306.
- Raviv A, Raviv A, Shimoni H, Fox NA, Leavitt LA. Children's self-report of exposure to violence and its relation to emotional distress. *Journal of Applied Developmental Psychology*. 1999; 20:337–353. doi:10.1016/S0193-3973(99)00020-9.
- Reich W. Diagnostic Interview for Children and Adolescents (DICA). *Journal of the American Academy of Child and Adolescent Psychiatry*. 2000; 39:59–66. doi:10.1097/00004583-200001000-00017. [PubMed: 10638068]
- Richardson GA, Conroy ML, Day NL. Prenatal cocaine exposure: effects on the development of school-age children. *Neurotoxicology and Teratology*. 1996; 18:627–634. doi:10.1016/S0892-0362(96)0012-3. [PubMed: 8947939]
- Richardson GA, Ryan C, Willford J, Day NL, Goldschmidt L. Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicology and Teratology*. 2002; 24:309–320. doi:10.1016/S0892-0362(02)00193-9. [PubMed: 12009486]
- Rose-Jacobs R, Augustyn M, Beeghly J, Martin B, Cabral HJ, Heeren TC, et al. Intrauterine substance exposures and Wechsler Individual Achievement Test-II scores at 11 years of age. *Vulnerable Children and Youth Studies*. 2012; 18:274–281. doi:10.1080/17450128.2011.648967.
- Roumell N, Wille D, Abramson L, Delaney V. Facial expressivity to acute pain in cocaine-exposed toddlers. *Infant Mental Health Journal*. 1997; 18:274–281.
- Scherling D. Prenatal cocaine exposure and childhood psychopathology: a developmental analysis. *American Journal of Orthopsychiatry*. 1994; 64:9–19. doi:10.1037/h0079494. [PubMed: 7511874]
- Shaffer A, Forehand R, Kotchick BA. A longitudinal examination of the correlates of depressive symptoms among inner-city African American children and adolescents. *Journal of Child and Family Studies*. 2002; 11:151–164. doi:10.1023/A:1015121424404.
- Shahinfar A, Fox NA, Leavitt LA. Preschool children's exposure to violence: relation of behavior problems to parent and child reports. *American Journal of Orthopsychiatry*. 2000; 70:115–125. doi:10.1037/h0087690. [PubMed: 10702856]
- Singer LT, Salvator A, Arendt R, Minnes S, Farkas K, Kliegman R. Effects of cocaine/polydrug exposure and maternal psychological distress on infant birth outcomes. *Neurotoxicology and Teratology*. 2002; 24:127–135. doi:10.1016/S0892-0362(01)00208-2. [PubMed: 11943500]

- Sood BG, Bailey BN, Covington C, Sokol RJ, Ager J, Janisse J, et al. Gender and alcohol moderate caregiver reported child behavior after prenatal cocaine. *Neurotoxicology and Teratology*. 2005; 27:191–201. doi:10.1016/j.ntt.2004.10.004. [PubMed: 15734270]
- Spence S, Najman JM, Bor W, O'Callaghan M, Williams GM. Maternal anxiety and depression, poverty and marital relationship factors during early childhood as predictors of anxiety and depressive symptoms in adolescence. *Journal of Child Psychology and Psychiatry*. 2002; 43:457–469. doi:10.1111/1469-7610.00037. [PubMed: 12030592]
- Stokes, ME.; Davis, CS.; Koch, GG. *Categorical data analysis using the SAS system*. SAS Institute; Cary: 2000.
- Straus MA. Leveling, civility, and violence in the family. *Journal of Marriage and the Family*. 1974; 36:13–29.
- Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. *American Journal of Psychiatry*. 2000; 157:1552–1562. doi:10.1176/appi.ajp.157.10.1552. [PubMed: 11007705]
- Thompson R, Briggs E, English DJ, Dubowitz H, Lee LC, Brody K, et al. Suicidal ideation among 8-year-olds who are maltreated and at risk: findings from the LONGSCAN studies. *Child Maltreatment*. 2005; 10:26–36. doi:10.1177/1077559504271271. [PubMed: 15611324]
- Tiesler CMT, Heinrich J. Prenatal nicotine exposure and child behavioural problems. *European Child & Adolescent Psychiatry*. 2014; 23:913–929. doi:10.1007/s00787-014-0615-y. [PubMed: 25241028]
- Tronick EZ, Frank DA, Cabral H, Mirochnick M, Zuckerman B. Late dose-response effects of prenatal cocaine exposure in newborn neurobehavioral performance. *Pediatrics*. 1996; 98:76–83. [PubMed: 8668416]
- Walthall JC, O'Connor MJ, Paley B. A comparison of psychopathology in children with and without prenatal alcohol exposure. *Mental Health Aspects of Developmental Disabilities*. 2008; 11:69–78.
- Wechsler, D. *Wechsler Intelligence Scale for Children-Third Edition (WISC-III)*. The Psychological Corporation; San Antonio: 1991.
- Youngstrom E, Izard C, Ackerman B. Dysphoria-related bias in maternal ratings of children. *Journal of Consulting and Clinical Psychology*. 1999; 67:905–916. doi:10.1037/0022-006X.67.6.905. [PubMed: 10596512]
- Zanis DA, McLellan AT, Corse S. Is the Addiction Severity Index a reliable and valid assessment instrument among clients with severe and persistent mental illness and substance abuse disorders? *Community Mental Health Journal*. 1997; 33:213–227. doi:10.1023/A:1025085310814. [PubMed: 9211041]

Table 1

Characteristics of birth mothers in original sample

Characteristic	Unexposed <i>n</i> =109	IUCE <i>n</i> =132	<i>p</i> value
Ethnicity (%)			
African-American and Caribbean	91	83	0.0466
Age, years (standard deviation)	24.8 (5.1)	27.4 (4.8)	0.0001
Education (%)			
Not high school	34	42	0.1301
High school	47	47	
Any college	19	12	
Marital status (%)			
Married	16	3	0.0012
Separated or divorced	9	8	
Never married	75	89	
First pregnancy (%)	43	30	0.0377

IUCE intrauterine cocaine exposure

Table 2

Sample characteristics by Intrauterine Cocaine Exposure (IUCE) status

Variables Mean (SD), % for categorical variables	N	Unexposed n=56	IUCE n=49	p value
Birth mother's characteristics				
African American/Caribbean ethnicity (% yes)	105	89 %	87 %	0.81
Age at child's birth	105	24.95 (5.17)	27.63 (3.98)	0.004
Education (years)	105	11.61 (1.58)	11.51 (1.24)	0.73
Marital status (% married)	105	17 %	2 %	0.01
First pregnancy (% yes)	105	50 %	31 %	0.04
Other substance use during pregnancy				
Average daily volume alcohol, last 30 days of pregnancy	105	0.002 (0.009)	0.900 (2.560)	0.01
Average daily number cigarettes smoked during pregnancy	105	2.54 (7.40)	7.98 (7.98)	0.001
Any prenatal marijuana use (bioassay or self-report; % yes)	105	11 %	37 %	0.002
Addiction Severity Index				
Alcohol composite (%>none)	103	12 %	63 %	<0.0001
Illicit drugs composite (%>none)	102	4 %	85 %	<0.0001
Family/Social composite (%>none)	105	50 %	55 %	0.60
Legal composite (%>none)	102	7 %	9 %	0.77
Medical composite (%>none)	105	14 %	22 %	0.28
Psychological composite (%>none)	103	20 %	38 %	0.04
Depressive symptoms				
Birth mother's CES-D total score (6-month visit)	90	11.59 (8.43)	10.34 (11.28)	0.55
Caregiver Characteristics (8.5-year visit)				
Substance use				
Average daily volume alcohol, past 30 days	101	0.56 (0.50)	0.53 (0.50)	0.79
Average daily number cigarettes smoked, past 30 days	101	0.34 (0.48)	0.44 (0.50)	0.32
Any marijuana use, past 30 days (% yes)	102	9 %	8 %	0.82
Psychological distress				
Brief Symptom Inventory: Global Severity Index	101	50.32 (11.26)	45.60 (11.41)	0.04
Family conflict				
Family conflict resolution scale total score	102	22.70 (5.51)	20.86 (4.62)	0.09
Addiction severity index				
Alcohol composite (%>none)	102	60 %	55 %	0.59
Illicit drugs composite (%>none)	102	19 %	18 %	0.95
Family/Social composite (%>none)	102	70 %	59 %	0.26
Legal composite (%>none)	102	25 %	24 %	1.00
Medical composite (%>none)	102	77 %	57 %	0.03
Psychological composite (%>none)	102	42 %	33 %	0.36
Parental incarceration (% any, within past 24 months)	92	20 %	10 %	0.16
Child characteristics				
Birth weight (grams)	105	3422.52 (521.13)	2932.67 (405.11)	<0.0001
Male (%)	105	55 %	59 %	0.69

Variables Mean (SD), % for categorical variables	<i>N</i>	Unexposed <i>n</i> =56	IUCE <i>n</i> =49	<i>p</i> value
Age (months) at 8.5-year DICA assessment	105	102.66 (3.53)	101.82 (2.37)	0.16
IQ (prorated WISC-III at 8.5-year visit)	102	88.79 (14.97)	86.18 (15.19)	0.38
VEX-R (highest quartile: %=yes)	86	20 %	37 %	0.09
Custodial arrangements at 8.5-year visit	102			<0.0001
Birth mother (%)		94 %	49 %	
Kinship care (%)		4 %	35 %	
Non-kinship foster care (%)		2 %	16 %	
Total number of caregiver changes by 8.5-year visit	104	0.52 (1.41)	2.15 (1.97)	<0.0001

CES-D Center for Epidemiology Studies-Depression scale, *DICA* Diagnostic interview for children and adolescents, *IUCE* Intrauterine cocaine exposure, *IQ* Intelligence quotient, *VEX-R* Violence exposure scale for children, Revised, *WISC-III* Wechsler Intelligence Scale for Children, Third Edition

Table 3

Unadjusted DICA psychiatric variables by Intrauterine Cocaine Exposure (IUCE) status

DICA variables	N	Unexposed n=56	IUCE n=49	p value
Total symptom counts mean (SD)				
Total symptoms	101	20.72 (11.76)	19.21 (13.40)	0.55
Total externalizing symptoms	101	9.87 (7.84)	8.04 (7.27)	0.23
Total internalizing symptoms	105	9.80 (7.68)	10.27 (9.13)	0.78
Depression: present	94	1.50 (1.74)	0.93 (1.47)	0.09
Depression: past	90	0.89 (1.30)	0.89 (1.63)	0.99
Separation anxiety disorder	94	1.00 (2.06)	1.36 (2.13)	0.41
Generalized anxiety disorder	87	2.23 (2.26)	2.14 (2.24)	0.86
Attention deficit hyperactivity disorder	101	7.08 (5.49)	6.25 (5.48)	0.45
Oppositional defiant disorder	100	1.89 (2.06)	1.28 (1.94)	0.13
Conduct disorder	100	0.91 (1.47)	0.55 (0.90)	0.16
Posttraumatic stress disorder (Parent + Child Report)	105	5.89 (5.49)	6.27 (5.32)	0.73
Diagnoses n (%)				
Any diagnosis	105	18 (32)	18 (37)	0.62
Any externalizing diagnosis	101	13 (25)	13 (27)	0.77
Any internalizing diagnosis	105	10 (18)	9 (18)	0.95
Depression: present	105	0 (0)	0 (0)	–
Depression: past	105	0 (0)	0 (0)	–
Separation anxiety disorder	94	1 (2)	2 (4)	0.61
Generalized anxiety disorder	87	2 (5)	1 (2)	1.00
Attention deficit hyperactivity disorder	101	6 (11)	7 (15)	0.62
Oppositional defiant disorder	100	10 (19)	7 (15)	0.60
Conduct disorder	100	4 (8)	1 (2)	0.37
Posttraumatic stress disorder (Parent + Child Report)	105	8 (14)	8 (16)	0.77
Number of diagnoses mean (SD)				
Total diagnoses	101	0.58 (0.95)	0.54 (0.85)	0.81
Total externalizing diagnoses	101	0.38 (0.74)	0.31 (0.55)	0.62
Total internalizing diagnoses	105	0.20 (0.44)	0.22 (0.51)	0.76

DICA Diagnostic Interview for Children and Adolescents, *IUCE* Intrauterine Cocaine Exposure

Table 4

Multivariate poisson regression models

Symptom counts	N	Rate ratio	95 % CI for rate ratio		p value
			Lower limit	Upper limit	
Outcome: Symptom total count	101				
Intrauterine cocaine (Exposed versus unexposed)		0.96	0.75	1.22	0.727
Caregiver ASI: Psychological composite @ 8.5 years (>0 versus 0)		1.50	1.17	1.92	0.001
Outcome: External symptom count	101				
Intrauterine cocaine (Exposed versus Unexposed)		0.95	0.66	1.37	0.791
Caregiver ASI: Psychological composite @ 8.5 years (>0 versus 0)		1.63			0.004
Birth mother ASI: Alcohol composite @ intake (>0 versus 0)		0.58	0.38	0.87	0.008
Birth mother ASI: Psychological composite @ intake (>0 versus 0)		1.54	1.10	2.16	0.011
Prorated WISC-III IQ @ 8.5 years (1 standard deviation change in IQ)		0.81	0.68	0.96	0.017
Outcome: Internal symptom count	105				
Intrauterine cocaine (Exposed versus unexposed)		0.94	0.66	1.32	0.716
Birth mother average daily alcohol use, 30 days preceding delivery (log transformation) @ intake		1.49	1.11	2.01	0.008
Caregiver ASI: Psychological composite @ 8.5 years (>0 versus 0)		1.54	1.10	2.14	0.011
Diagnoses	N	Rate Ratio	95 % CI for Odds Ratio		p value
			Lower	Upper	
Outcome: Total diagnosis count	101				
Intrauterine cocaine (Exposed versus unexposed)		1.50	0.81	2.78	0.202
Caregiver ASI: Psychological composite @ 8.5 years (>0 versus 0)		2.39	1.34	4.26	0.003
Birth mother ASI: Alcohol @ intake (>0 versus 0)		0.37	0.17	0.79	0.010
Outcome: External diagnosis count					
Intrauterine cocaine (Exposed versus unexposed)	101	1.22	0.61	2.45	0.571
Caregiver ASI: Psychological composite @ 8.5 years (>0 versus 0)		3.03	1.54	5.98	0.001
Birth mother ASI: Alcohol @ intake (>0 versus 0)		0.41	0.17	0.97	0.042
Child prorated WISC-III IQ @ 8.5 years (1 standard deviation change in IQ)		0.69	0.49	0.99	0.043
Outcome: Internal diagnosis count	105				
Intrauterine cocaine (Exposed versus unexposed)		0.78	0.34	1.75	0.540
Birth mother average daily alcohol use, 30 days preceding delivery (log transformation) @ intake		2.09	1.28	3.43	0.003

ASI Addiction Severity Index, IUCE Intrauterine Cocaine Exposure, IQ Intelligence Quotient, WISC-III Wechsler Intelligence Scale for Children, Third Edition