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Pre- and postnatal tobacco and cannabis exposure and child behavior problems: Bidirectional associations, joint effects, and sex differences

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Abstract

Aims—We examined prospective associations between pre-and-postnatal tobacco and cannabis exposure on child behavior problems from 2 to 3 years of child age, sex differences in these associations, and bidirectional associations between maternal postnatal substance use and child behavior problems across time.

Methods—The sample consisted of 247 primarily young, unmarried, low-income, minority mothers and their children (97 prenatally exposed to tobacco and cannabis, 81 exposed to tobacco only, and 69 non-exposed). Mothers were assessed during each trimester of pregnancy, at 2, 9, 16 months, 2 and 3 years of child age.

Results—Bivariate results indicated significant differences mainly for girls. Girls in the prenatal tobacco exposure group had higher internalizing problems compared to the other two groups, and higher attention and sleep problems at 3 years compared to the control group. Higher number of cigarettes per day during pregnancy was significantly associated with higher anxiety/depression and higher attention problems at 3 years, and the associations were stronger for girls compared to boys. In model testing controlling for prenatal exposure, results indicated bidirectional associations between behavior problems at 2 years and maternal postnatal cannabis use, such that higher cannabis use across the infant toddler period predicted higher behavior problems at 2 years, which in turn predicted higher cannabis use a year later.

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Conflict of Interest

None

Conclusions—Results add to the literature on joint effects of tobacco and cannabis, highlight the importance of considering bidirectional associations between maternal substance use and child behavior problems, and indicate generally stronger prenatal tobacco exposure effects for girls.

Keywords

Tobacco; Cannabis; Child Behavior Problems; Prenatal Substance Exposure

1. Introduction

1.1 Prenatal substance exposure

The prenatal period is a time of enhanced vulnerability during which a variety of exposures, including maternal tobacco and cannabis use, have long-term impacts on both physical and behavioral development (USDHHS, 2014). Tobacco use in the form of cigarettes continues to be one of the most commonly used drugs in pregnancy and delivers significant amounts of chemical toxins to the fetus via maternal bloodstream (USDHHS, 2014). Tobacco use is often comorbid with cannabis and the two substances are often smoked together (El Marroun et al., 2008; USDHHS, 2014; Passey et al., 2014). Approximately 10% of pregnant women have reported using cannabis in recent years, with the majority being daily users (Ko et al., 2015). These rates are much higher among pregnant tobacco smokers (Passey et al., 2014). In addition, the amount of THC in cannabis has increased substantially over the past two decades (Calvigioni et al., 2014; Mehmedic et al., 2010), making newer studies of developmental outcomes increasingly imperative, especially when combined with comorbid tobacco use.

Although tobacco and cannabis are often used together, the combined effect of both on child behavior problems has seldom been examined. Often, the association between prenatal exposure to one substance and a particular child outcome is examined while statistically controlling for the impact of the other (see Huizink, 2015, review). While this is important in order to understand the unique variance accounted for by a particular substance, it does not reflect the reality of co-occurring exposure to both substances. In addition, most women who use substances during pregnancy continue to use during the postnatal period, and postnatal exposure to substances such as tobacco and cannabis may also have significant effects on behavior problems (Bada et al., 2011; Day et al., 2000). Higher child behavior problems may in turn be causally related to increased maternal substance use postnatally (Pelham and Lang, 1999). However, few studies have examined potential bidirectional associations between child behavior problems and continuity of maternal substance use postnatally.

The purpose of this study was to examine prospective associations between maternal tobacco and cannabis use from pregnancy to 3 years postpartum and changes in child behavior problems from 2 to 3 years of child age, using a high-risk, diverse sample consisting of young, low-income urban women with low education. In addition to prenatal and postnatal tobacco exposure, we examined the joint effect of tobacco and cannabis use and bidirectional associations between substance use and child behavior problems across time. We tested a conceptual model that included prenatal exposure effects, stability/change over time in maternal substance use and child behavior problems, as well as prospective,

bidirectional associations. We addressed some of the methodological limitations in many previous studies by using a prospective design beginning in the first trimester of pregnancy with multiple measures of substance use including biochemical verification and recruiting a demographically similar control group.

1.2 Prenatal tobacco and cannabis exposure effects on behavior problems

A large body of literature has examined the association between maternal tobacco use during pregnancy and child behavior problems. However, many of these studies have methodological flaws such as inadequate control groups that do not account for demographic differences between substance using and comparison women, reliance on retrospective data, the use of single-item measures to assess substance use during pregnancy, and failure to use biochemical verification of substance use (e.g., Monshouwer et al., 2011). Recognizing these shortcomings, other studies using more sophisticated research designs with better controls for demographic differences, prospective designs, and use of biomarkers for exposure assessment in addition to more intensive self-reports have reported higher behavior problems among tobacco exposed children (Cornelius and Day, 2009; Weibe et al., 2015). Indeed, a recent review of the literature concluded that there is robust evidence for the association between prenatal tobacco exposure and problem behavior in children (USDHHS, 2014, review). One explanation for this association is the potential teratological effect of chemical compounds in cigarettes, nicotine, and nicotine metabolites on fetal development. Results from animal studies provide support for nicotine as a neuroteratogen, impacting the fetal nervous system development, including neurons that control attention and arousal (Mamiya, Buchanan, Wallace, Skinner, and Garcia-Rill, 2005). Genetically informed designs such as twin and children of twin designs indicate small but independent effect of prenatal tobacco exposure on ADHD behavior, but a reduction in the prenatal effect after consideration of genetic factors for conduct disorder (see Huizink, 2009, review).

The literature on cannabis exposure and behavior problems is much smaller. Results from the Maternal Health Practices and Child Development (MHPCD) study indicate significant effects of prenatal cannabis exposure on sleep, cognitive functioning including reasoning and memory, attention, impulsivity, and depression/anxiety across development (see Day et al., 2011). Recently, results from this cohort study indicated significant indirect effects of prenatal cannabis exposure on delinquency in early adolescence via lower attention and higher depressive symptoms in middle childhood (Day et al., 2011). These domains of cognitive functioning were also implicated in the Ottawa Prenatal Prospective Study (Fried and Watkinson, 1990). Few studies have examined the combined effects of tobacco and cannabis exposure on child behavior.

1.3 Sex differences

There are theoretical reasons to expect potential sex differences in response to prenatal tobacco and cannabis exposure. For example, there are sex differences in the development and functions of the endocannabinoid system (Craft, Marusich, and Wiley, 2013). However, there has not been a systematic examination of potential sex differences in prenatal tobacco (Coles et al., 2012) or cannabis exposure literature (Willford et al., 2012). Moreover, when sex differences were examined, the results have been mixed ranging from no sex differences

in tobacco exposure effects (see Coles et al., 2012; El Marroun et al., 2011), sex differences in control but not tobacco exposed children (Johnson et al., 2009), and higher behavior problems for cannabis exposed girls (El Marroun et al., 2011).

Another complicating factor is the failure to distinguish pre- and post-natal exposure. Given continuity of exposure from prenatal to the postnatal period in most families and the potential for second hand exposure for both tobacco and cannabis, the role of continued postnatal exposure may be critical.

1.4 Continued postnatal exposure and bidirectional associations

Few studies have examined bidirectional associations between continued maternal substance use and child behavior. However, some studies have examined parental postnatal substance use as predictors of child behaviors (e.g., Bada et al., 2011; Day et al., 2000; Delaney-Black et al., 2011). Prenatal cocaine and postnatal tobacco use were predictive of higher externalizing behavior problems in children (Bada et al., 2011), and both prenatal and postnatal cocaine use were uniquely predictive of adolescent cocaine use at 14 years of age (Delaney-Black et al., 2011). In a study of children in an asthma intervention trial, current child cotinine levels were associated with behavior problems only among boys (Yolton et al., 2008), suggestive of post-natal exposure effects. Recently, in a study of infants hospitalized with bronchiolitis, 16% had detectable levels of THC in urine. Among infants with >2.0 ng/mL of cotinine, a primary metabolite of nicotine in urine, 56% were also urine positive for THC, highlighting the continuity of postnatal exposure and the comorbid nature of exposure to tobacco and cannabis (Wilson et al., 2017).

In addition to these studies indicating a potential causal role of postnatal exposure on child behavior problems, difficulties in managing child behavior problems may also increase maternal postnatal substance use. There is supportive evidence for this hypothesis from a landmark series of studies using an experimental design. In these studies, experimenters manipulated child behavior and examined changes in subsequent maternal alcohol consumption (see Pelham and Lang, 1999). Results indicated that mothers exhibited greater physiological and subjective distress after interacting with ADHD children compared to control children, and consumed more alcohol. Taken together with the small literature on postnatal exposure effects, this set of studies provides support for both parent influences on child behaviors as well as child influences on parental substance use. However, to our knowledge, the potential for bidirectional associations have not been examined in any single study.

1.5 Aims and hypotheses

Based on this literature, we examined differences in child behavior problems across three prenatal exposure groups, non-exposed (NE) children, children exposed only to tobacco (PTE), and children exposed to both tobacco and cannabis (PTCE). We hypothesized that children in both the PTE and PTCE groups would display more behavior problems compared to NE group, with stronger effects for children exposed to both substances. Next, we examined associations with trimester of exposure and dose-response associations. Finally, we examined a conceptual model predicting changes in child behavior problems

from 2 to 3 years of age. We hypothesized that prenatal exposure to tobacco only, and the combination of tobacco and cannabis may have different associations with continuity of these substances in the postnatal period and with child behavior problems. We tested a model examining prenatal exposure effects, stability in continued prenatal to postnatal use of tobacco and cannabis, and stability in child behavior problems from 2 to 3 years of child age. We expected prenatal exposure to tobacco and cannabis to have stronger effects on behavior problems than tobacco exposure alone. We also expected these maternal and child behaviors to have moderate stability. Next, we hypothesized that postnatal exposure would predict higher child behavior problems and vice versa. Thus, we examined potential bidirectional associations using time-lagged pathways from maternal substance use to child behavior problems and from child behavior problems to continued maternal substance use, after accounting for within time associations. Finally, we examined if there were sex differences in these pathways. Given the scant literature on sex differences, we did not have specific hypotheses regarding direction of associations, but explored the possibility of potential sex differences in hypothesized bidirectional associations between maternal substance use and child behavior problems. Finally, we excluded heavy alcohol use by design given the large literature on significant teratologic effects of alcohol on child development.

2. Method

2.1 Sample selection

Women who presented for prenatal care at a large city hospital were asked to complete a self-report screening form during their first prenatal appointment. Of the 3583 women who completed the screening form, 1671 (47%) met initial eligibility criteria. Eligibility criteria included maternal age over 18 years, women were between 12 and 20 weeks gestation, no multiple births, English speakers, and to rule out the effects of other substances: no illicit drug use other than cannabis, no heavy alcohol use (more than 1 drink/day on average or more than four drinks on one occasion). Of these, 404 (24%) completed at least one prenatal interview. Among the 76% of women who were eligible based on the screening form but were not recruited, approximately 60% were non-smokers and were not demographically similar to a recruited smoker, and about 17% were quitters. About 23% were tobacco smokers who had incorrect contact information or were scheduled but did not show for their first prenatal interview within the first 20 weeks of pregnancy, had an abortion or miscarriage, were not interested, or did not speak English. Among the 404 women who were interviewed prenatally, 94 could not be located after delivery, were no longer interested, or did not keep their postnatal appointment within the target dates. Of the 404 women, 258 met final eligibility criteria after delivery (infant able to medically comply with procedures at delivery) and were assessed at 2 months of infant age. Of these 258 mother-infant dyads, 5 (2%) were closed due to infant death, infant unable to comply with procedures, or custody loss. An additional participant was closed because the father refused participation after delivery, and one additional participant was dropped because infant meconium was positive for methamphetamine, resulting in a final sample of 251 mother-infant dyads. Of these 251 mother-infant dyads, four were not included in analyses because they were users of cannabis only, and not tobacco, resulting in a final sample of 247 participants. There were no

demographic differences between the eligible 404 and the final 247 participants in our sample, with correlations ranging from $r = -.07$ to .07. Tobacco smokers were oversampled so that one non-smoker was recruited for every two smokers to facilitate inclusion of the full range of light to heavy smokers to maximize power to examine potential dose response relationships.

2.2 Participants

Participants included 247 mothers and their infants recruited prenatally. Of these dyads, 103 (51 boys and 52 girls) were infants prenatally exposed to tobacco and cannabis, 75 (47 boys and 28 girls) infants were prenatally exposed to tobacco only, and 69 (33 boys and 36 girls) were infants not exposed to tobacco or cannabis.

Mothers ranged in age from 18 to 39 (M = 24.09, SD = 5.00) at the first appointment. Maternal race was 51% African-American, 31% Caucasian, 19% Hispanic (8% Hispanic White, 11% Hispanic Black, and 81% only identifying race/ethnicity as Hispanic), and 8.1% other or mixed race, with several identifying as more than one race. Forty-six percent of the women were married or living with their partner, 32% were in a relationship, but not living with their partner, 21% were single, and 1% were divorced. Twenty-nine percent of women had less than a high school education, 29% completed high school, 28% completed some college, 9% had a vocational/technical or associates degree, and 4% had a bachelor's degree. Therefore, the sample overall consisted primarily of young, unmarried, low-income, minority women with low education.

2.3 Procedure

Informed written consent was obtained from interested, eligible women. Prenatal assessments were conducted once in each trimester of pregnancy, and child assessments were conducted at 2, 9, 16 months, and 2 years of child age. A phone interview was conducted with the mothers at 3 years of child age. Data from the prenatal interviews, from maternal interviews and infant saliva samples at 2, 9, 16 months, and 2 year visits, and from the maternal phone interview at 3 years were included in these analyses. Participants received payments for completed assessments at all visits.

2.4 Maternal prenatal substance use

Maternal cigarette and cannabis use during pregnancy was assessed using a combination of maternal self-report, maternal saliva samples taken at each trimester of pregnancy, and infant meconium. At each prenatal and postnatal interview, the Timeline Follow-Back Interview (TLFB; Sobell and Sobell, 1992) was used to gather daily tobacco, alcohol, and cannabis use for the previous three months (Brown et al., 1998). Mothers were assigned to the PTE group if they acknowledged smoking during pregnancy, if maternal saliva samples were positive for cotinine at or above 10 ng/mL, or if infant meconium was positive for cotinine, nicotine, or trans-3′ hydroxycotinine (OHCOT). Maternal saliva specimens were analyzed by the U.S. Drug Testing Laboratory (Des Plaines, IL) for D9–tetrahydrocannabinol (THC), the psychoactive component of marijuana, by immunoassay screening (4.0 lg/L cutoff) and gas chromatography-mass spectrometry GC-MS confirmation (4.0 lg/L cutoff) and for cotinine using liquid chromatography–tandem mass spectrometry (LC–MSMS) for majority of cases

(with the exception of the first 32 women recruited into the study who had trimester 1 saliva samples assayed using ELISA at 10 ng/mL). The meconium samples were assayed with a validated LC– MSMS method (Gray et al., 2010a) at 2.5 ng/g nicotine, 1 ng/g cotinine, and 5 ng/g OHCOT. Meconium samples were also assayed with a validated two-dimensional GC-MS method for THC, 8b, 11-dihydroxy-THC, 11-nor-9-carboxy-THC, and cannabinol (Gray et al., 2010b). Participants were assigned to the PTCE group if they self-reported cannabis use during pregnancy, if infant meconium tested positive for cannabis, or if maternal saliva was positive for cannabis in any of the 3 trimesters. Mothers who were positive on tobacco, cannabis, or both based on any of the measures were assigned to the tobacco or both tobacco and cannabis group.

2.5 Postnatal tobacco exposure

Postnatal tobacco exposure was assessed for infants during their 2, 9, 16 months, and 2 year visit using infant saliva samples. Infant saliva samples were analyzed for cotinine levels. Salivary cotinine concentrations are highly correlated with those in the blood (Jarvis, Primatesta, Erens, Feyerabend, and Bryant, 2003) and, thus, are an accurate yet noninvasive way of measuring ETS exposure. Saliva samples were collected by placing eye spears (BD Opthalmology “Visispears” [product #581089], marketed by Salimetrics as “Sorbettes” [product #5029]) in the mouth of infants. These samples were placed in a storage vial, immediately placed in −80C freezer, and sent to the Center for Interdisciplinary Salivary Bioscience for assay. The advantage of saliva testing is that it quantifies exposure to cigarette smoke from all possible sources including other household smokers. Cotinine levels for 2, 9, and 16 months of child age were significantly correlated (ranging from $r = .18$ to .53, $p < .05$) and averaged in order to provide a measure of infant postnatal exposure across early childhood. Maternal reports using the TLFB were used at 3 years, since no saliva samples were collected at this time point.

2.6 Maternal postnatal cannabis use

Maternal cannabis use per day was assessed using the TLFB. Mothers were asked during their 2, 9, 16 months, 2 and 3 year visits to recall their cannabis use since their previous visit. Women who smoked blunts were asked how many joints could be rolled from the amount of cannabis in each blunt. The number of joints smoked per day at 2, 9, and 16 months of child age were significantly correlated (ranging from $r = .31$ to .77, $p < .001$) and averaged in order to provide an overall estimate of postnatal exposure across early childhood.

2.7 Child problem behavior

Toddler problem behavior was assessed using maternal report on the Child Behavior Checklist for ages 1 ½–5 (CBCL; Achenbach and Rescorla, 2000) at 2 and 3 years of child age. The CBCL is a widely used measure of children’s internalizing and externalizing problems. It consists of 100-items and is rated on a three-point response scale ranging from “not true” to “very true,” with some open-ended items designed to elicit detailed information about a particular problem behavior. Higher scores indicate more child behavior problems. Specifically, the subscales of sleep problems, internalizing problems, and externalizing problems were used. Reliability for this sample was acceptable for sleep problems, with

internal consistency of α = .71 at both two and three years, good for internalizing problems (α = .84 at both two and three years), and excellent for externalizing behavior (α = .91 at both two and three years).

2.8 Analytic strategy

We first examined associations among the different prenatal substance exposure variables, postnatal exposure, and child behavior problems using Pearson correlations or ANOVAs as appropriate. These included the smoking group status variable that was a combination of all indices of PTE, the cannabis group status variable that was a combination of all indices of cannabis exposure, the dose response variables of the average number of cigarettes and joints per day, and the timing of exposure variables of the average number of cigarettes and joints per day in each trimester of pregnancy. Analyses of potential confounds were conducted next using correlations or ANOVAs as appropriate. Group differences and sex-related differences were examined using correlations or ANOVAs/MANOVAs as appropriate.

We then tested a confirmatory factor model for child behavior problems at 2 and 3 years. We used Structural Equations Modeling (SEM) to test the hypothesized model with prenatal exposure as the exogenous variables, continued postnatal use of tobacco and cannabis and latent variables for child behavior problems as endogenous variables. Multiple group analyses were used to examine moderation by sex. Nested χ^2 difference tests were used to test equality constraints of path coefficients across gender. The $\Delta\chi^2$ was used as an omnibus test of differences across child sex. SEM analyses were conducted in Mplus 7.4 (Muthen and Muthen, 1998–2015) using full-information maximum likelihood estimation procedures, which can provide accurate parameter estimates and standard errors with missing data (Arbuckle, 1996).

2.9 Missing data

As expected in any longitudinal study, there were some incomplete data for some of the participants at one or more of the four assessment points included in this study. Of the eligible mother-infant dyads who completed the prenatal assessments, 198 had complete meconium data and 247 completed the 2-month assessments. Five participants were missing at 9 month assessments, 9 participants were missing at 16 month assessments, 15 participants were missing at 2 year assessments, and 41 participants were missing at 3 year assessments. There were no significant differences between families with complete vs. missing data on any of the variables included in this study and demographics at any age.

3. Results

3.1 Group differences in demographics and maternal substance use

Descriptive data for demographics and substance exposure are presented in Table 1. There were a higher percentage of Caucasian mothers in both the PTE and PTCE groups compared to the control group. Mothers in the exposure groups also had more smoking partners.

Descriptive data for demographics and substance exposure for boys and girls separately are presented in Table 1. Girls in the control group were breastfed longer compared to those in the other two groups. Among boys, there were a higher percentage of Caucasian mothers in both the PTE and PTCE groups compared to the control group. Mothers of girls in the PTCE group had higher percentage of smoking partners compared to the other two groups. Among boys, mothers in both the PTE and PTCE groups had higher percentages of partners who smoked.

3.2 Substance exposure and child behavior problems

There were no differences in child behavior problems by exposure status for the sample as a whole. However, analyses conducted for boys and girls separately indicated several group differences for girls, but not boys. As noted in Table 2, girls in the PTE group were more emotionally reactive, anxious/depressed, withdrawn, and exhibited higher levels of total internalizing problems at 3 years than those in the other two groups. Girls in the PTE group also had more attention problems and sleep problems compared to the control group. There were no significant group differences at 2 years.

Approximately 10% of toddlers were in the borderline or clinical range for internalizing problems at 2 years and 9% were in this range at 3 years. Approximately 11% were in the borderline or clinical range for externalizing problems at 2 years, and 9% were in this range at 3 years. There was a significant association between group status and clinical status for child internalizing behavior problems at 3 years, $\chi^2(2) = 6.68$, $p = .03$. Among the children in the clinical or borderline range at 3 years, 57% were in the PTE group, compared to 23% in the control group and 20% in the PTCE group.

Among girls, about 10% of them were in the clinical or borderline range for internalizing problems at 24 months and 6% were in this range at 36 months; 14% of girls were in the borderline or clinical range for externalizing problems at 24 months, and 8% were in this range at 36 months. In addition, girls' clinical status for internalizing problems at 36 months differed by their group status, $\chi^2(2) = 9.71$, $p = .01$, such that 71% of those who met clinical criteria were in the PTE group and the remaining in the control group. Among boys, 10% were in the clinical or borderline range for internalizing problems at 24 months and 11% were in this range at 36 months; 9% of boys were in the borderline or clinical range for externalizing problems at 24 months, and 11% were in this range at 36 months. There was no association between group status and clinical status for internalizing problems at 36 months for boys.

Next, we examined dose-response associations using the continuous measures of exposure in each trimester separately, exposure averaged across pregnancy, and fetal exposure based on meconium assays. At 2 years, higher first trimester cannabis use was associated with higher symptoms of anxiety/depression ($r = .14$, $p = .05$). At 3 years, mothers who smoked more in the first ($r = .15$, $p = .04$) and third ($r = .15$, $p = .04$) trimesters, and those who smoked more on average across pregnancy ($r = .15$, $p = .04$) reported higher symptoms of child anxiety/depression. Mothers who smoked more cigarettes in the first trimester and across pregnancy also reported higher child attention problems ($r = .18$, $p = .01$ and $r = .15$, $p = .04$, respectively).

Correlational analyses for boys and girls separately at 2 years indicated only one significant association for girls. Among girls, those with positive meconium for cannabis had fewer sleep problems ($r = -.22$, $p = .05$). However, correlational analyses indicated more consistent associations between continuous measures of substance use and child behavior problems at 3 years as noted in Table 3. For girls, mothers who smoked more cigarettes in each trimester and averaged across pregnancy reported higher symptoms of child anxiety/depression; higher cannabis in meconium was related to lower somatic symptoms at 3 years. For boys, mothers who smoked more cigarettes in the 1st and 3rd trimesters and averaged across pregnancy reported higher attention problems.

Finally, for the sample as a whole, both child behavior problems and postnatal maternal substance use were found to be moderately stable from 2 to 3 years of child age. Toddler salivary cotinine at 2 years reflecting postnatal exposure was concurrently associated with child externalizing problems ($r = .15$, $p = .04$). When separate analyses were conducted for boys and girls, the patterns of stability for both postnatal exposure and child problem behavior remained unchanged (see Table 4). For girls but not boys, higher average infant/toddler salivary cotinine was significantly correlated with greater sleep and externalizing problems at 2 years; higher toddler (2 years) salivary cotinine was associated with greater externalizing problems and anxiety/depression at 3 years; and toddler withdrawn behavior was correlated with higher maternal cannabis use at 3 years of child age.

Mothers who breastfed for longer durations were less likely to use tobacco postnatally at 3 years of child age ($r = -.15$, $p = .04$), and reported lower externalizing problems in their children ($r = -.20$, $p = .001$) at 3 years. Thus, days of breastfeeding during infancy was used as a covariate in model testing. Given gender differences in associations among variables, child gender was also included as a covariate when testing the model for the full sample, and examined as a moderator of associations among variables using multiple group analyses thereafter.

3.3 Model testing

3.3.1 Measurement model—Confirmatory factor analyses (CFA) were conducted first to examine the fit of a measurement model with sleep, internalizing, and externalizing problems as indicators for a latent construct of *child problem behavior*, separately for 2 and 3 years. Given that the covariance for both models was just-identified (the number of free parameters equals the number of observations, degrees of freedom = 0; Kline, 2015), an equality constraint was imposed on error variances of *externalizing problems* and *internalizing problems* in order to resolve the issue of model just-identification. At both 2 and 3 years, this model fit the data well, $\chi^2(1) = 1.85$, $p = .174$; CFI = 1.00; RMSEA = .06 (90% CI = .00, .22), SRMR = .02 at 2 years, and $\chi^2(1) = 1.28$, $p = .258$; CFI = 1.00; RMSEA = .04 (90% CI = .00, .20), SRMR = .01 at 3 years. The three factor loadings ranged from .64 to .91, ps < .001 at 2 years and from .51 to .91, ps < .001 at 3 years. These two latent variables were then included in the hypothesized structural model as depicted in Figure 1. The use of latent variables has the advantages of model parsimony and allowing for estimates of model effects that are adjusted for measurement errors of the latent constructs (e.g., Cohen, Cohen, West, and Aiken, 2003).

3.3.2 Structural model—We tested the hypothesized model in two steps. The first model (Model 1) included the stability paths for maternal substance use and child behavior problems across time, as well as the prospective causal paths from prenatal substance exposure to child behavior problems. Cross-lagged paths between maternal postnatal substance use and child behavior problems were added in the next step (Model 2). Model 1 did not have an adequate fit, $\chi^2(88) = 371.10$, $p < .001$; CFI = .77; RMSEA = .11, 90% CI: .10– .13; SRMR = .09. Although there were bivariate associations between prenatal substance exposure and child problem behavior at 3 years, with 2 year problem behavior in the model, adding such direct paths did not improve model fit. Modification indices suggested the addition of two theoretically meaningful parameters, which were included in the model one at a time. The first was a direct path between maternal postnatal cannabis use (number of joints per day) in the infant/toddler period to cannabis use at 3 years. The second was a path from prenatal PTE to number of cigarettes per day at 3 years. The addition of these two stability paths improved model fit and this revised model fit the data adequately, $\chi^2(86) = 206.10$, $p < .001$; CFI = .90; RMSEA = .08, with 90% CI .06 – .09; SRMR = .07.

The bidirectional model (Model 2) was examined in the next step. Six cross-lagged paths between maternal postnatal substance use and child behavior problems were added to the model. This resulted in a significant improvement in fit, $\Delta\chi^2$ (6) = 12.68, $p < .05$. Higher average postnatal cannabis use in the infant/toddler period was prospectively predictive of higher child behavior problems at 2 years of child age, which in turn was prospectively predictive of higher average maternal cannabis use at 3 years. This model explained 53% of the variance in problem behavior at 3 years. The model also explained 53% of the variance in maternal tobacco use and 66% of the variance in maternal cannabis use at 3 years postpartum.

3.4 Moderating effects of child sex

We conducted multiple group analyses to determine if stability or bidirectional associations varied by child sex. First, measurement invariance for the construct of child problem behavior for boys and girls was established[1]. To examine if the hypothesized structural paths may be different for boys and girls, we conducted two multiple-group models following the same steps as for the full sample[2]. The first examined the prenatal exposure effects and stability paths for maternal substance use and child behavior problems, and the second added the cross-lagged paths. Three stability paths in the model were found to differ by child sex, $\chi^2(159) = 329.21$, $p < .001$. The stability path for maternal cannabis use from 2 to 3 years was stronger for girls ($\beta = .82$, 95% CI [.67, .93], $p < .001$) than for boys, $\beta = .46$, 95% CI [.30, .58], $p < .001$. However, there was a direct path from maternal cannabis use in the infant/toddler period to the preschool period for boys ($\beta = .48$, 95% CI [.32, .60], $p < .001$), but not girls, $\beta = -.04$, 95% CI [−.26, .12], $p = .592$. Finally, boys demonstrated more stable problem behaviors from toddler to preschool age ($\beta = .79$, 95% CI [.64, .90], $p < .001$) than

[1]Given that, in a multiple-sample CFA, it is more approriate to analyse unstandarized factors (e.g., fix the unstandarized loading of the same indicator to 1.0 in each group) than to scale the factors (Kline, 2005), the multiple group CFA models were reanalysed by fixing the loadings of different indicators to 1.0 each time to ensure that all of the three indicators of the same construct were measured in comparable ways among boys and girls. The findings were similar across different analyses.

[2]Analyses using the individual subscales of *attention problems* and *aggressive behavior* yielded findings that were similar to those obtained with the latent variables reflecting overall child behavior problems.

did girls, β = .56, 95% CI [.32, .74], $p < .001$. There was also a sex difference in the cross-lagged path from infant/toddler salivary cotinine to problem behavior at 2 years, $\chi^2(158) = 314.8$, $p < .001$. Higher postnatal tobacco exposure was associated with higher behavior problems among girls (β = .26, 95% CI [−.01, .46], $p = .01$) but not boys, β = −.11, 95% CI [−.41, .11], $p = .33$.

4. Discussion

One goal of this study was to examine associations between tobacco and co-occurring tobacco and cannabis exposure associations with child behavior problems, and sex differences in these associations. Results for the sample as a whole indicated no differences by prenatal substance exposure status in frequency of behavior problems at either the toddler or the preschool age. However, there were significant differences for girls at 3 years of age, such that girls in the PTE group had higher internalizing problems compared to the other two groups, and had higher attention and sleep problems at preschool age compared to the control group. In general, studies of prenatal tobacco exposure have largely ignored sex differences (Coles et al., 2012). In the few studies that have examined sex differences, results have been mixed. For instance, in a prospective study with demographic controls and biomarkers of use, there were significant sex by tobacco exposure interactions on maternal reports of externalizing and total behavior problems at 2 years. However, this was because of higher behavior problems among boys compared to girls within the control group, but no sex differences in the tobacco exposure group (Johnson, Lynch, Kable, and Coles, 2009). In a study of prenatal cannabis exposure, with a large proportion of these children also exposed to tobacco, El Marroun et al. (2011) noted significantly higher attention and aggression problems among cannabis exposed girls but not boys at 18 months of child age, but no differences from controls among those who were exposed to tobacco alone. No information was provided about the amount or timing of exposure. Studies of self-regulation, a construct etiologically salient for child behavior problems, indicate significant associations between PTE and self-regulation among boys at 3 years, but not girls (Wiebe et al., 2015). In contrast to these sex differences, others have reported no interactions between tobacco exposure and child sex on externalizing problems including aggression at 3 (Orlebeke et al., 1999) and 5 years (Williams et al., 1998) with both boys and girls in the PTE groups having higher externalizing problems compared to controls. Similarly, Hutchinson and colleagues (Hutchinson et al., 2010) reported higher conduct problems among PTE exposed boys and girls at 3 years of age, but higher hyperactivity-inattention only among PTE exposed boys, but not girls compared to non-exposed children. As noted in the review by Coles et al. (2012), most studies on tobacco exposure have not focused on potential sex differences and thus the literature on sex differences is small; taken together, results are mixed. Results highlight the importance of sex as a moderator of prenatal exposure effects, but there is little clarity regarding direction of the sex difference. There is a need to examine this issue using prospective designs that can address timing and dose questions. Mixed findings may also be due to differences in samples, co-occurring risks, and developmental timing for assessment of child behavior problems.

There were significant dose-response associations with tobacco for the sample as a whole, with higher number of cigarettes per day during pregnancy associated with higher anxiety/

depression and higher attention problems at 3 years of child age. There were stronger dose-response associations with anxiety/depression among girls, and stronger associations for attention problems among boys. With regard to timing of exposure for the sample as a whole, first trimester tobacco exposure was most consistently associated with higher attention problems. Both first and third trimester tobacco exposure and first trimester cannabis exposure were associated with higher anxiety/depression, although there were differences in timing of associations. These results are consistent with previous studies that indicate stronger first trimester effects on child behavior problems, including depressive symptoms for both tobacco (Cornelius et al., 2011) and cannabis (Day et al., 2011; Gray et al., 2005). One explanation for these consistent first trimester effects of tobacco may be that fetal nicotinic acetylcholine receptors are present in the first trimester. Activation of these receptors by nicotine changes the expression of these receptors and the modulating function of these receptors on neurotransmitters such as dopamine, norepinephrine, and serotonin (see Smith et al., 2010). Similarly, animal studies provide ample evidence that prenatal exposure to cannabinoids impacts the endocannabinoid system present in the brain in early fetal development and thereby alters the maturation of similar neurotransmitter systems (Campolongo et al., 2011). These neurotransmitter systems play a critical role in regulating affect. Another explanation for these first trimester effects may be that for the majority of women, level of substance use is highest in the first trimester (Eiden et al., 2013), and first trimester associations may reflect the potential effect of higher level of exposure.

One goal of this study was to examine a conceptual model of potential bidirectional associations between maternal substance use and child behavior problems in addition to examining potential group differences between PTE and PTCE children compared to controls. Results indicated some bidirectional associations, and there were some sex specific effects. When considering the sample as a whole, results indicated prospective, bidirectional associations between behavior problems at 2 years and maternal postnatal cannabis use. Higher maternal cannabis use across the infant toddler period was predictive of higher behavior problems at 2 years, which was prospectively predictive of higher maternal cannabis use a year later, even after accounting for within time associations and stability in cannabis use across time. The pathway from child behavior problems to higher maternal cannabis use may be interpreted as mothers using cannabis as a coping strategy. These results are generally supportive of laboratory studies of higher maternal alcohol use and subjective distress when faced with an ADHD compared to non-ADHD child (Pelham and Lang, 1999). However, it is important to note that the effect sizes were in the small range, although these associations reflected unique pathways, since they were controlling for prenatal substance use as well as stability in maternal substance use over time.

An additional predictive pathway from postnatal infant/toddler tobacco exposure (controlling for prenatal exposure) to higher behavior problems at 2 years was significant for girls, but not boys. These results are generally supportive of previous studies indicating associations between postnatal tobacco exposure and higher behavior problems at 3 years of child age, such as impulsivity and peer problems (Day et al., 2000). Results are also similar to those reported by Bada et al. (2011) indicating significant associations between postnatal tobacco exposure and increases in externalizing behavior problems from 7 to 11 years of age, although neither of these studies reported sex differences.

This study adds to the larger literature on prenatal exposure effects, particularly the effects of polysubstance abuse given the large comorbidity of tobacco and cannabis use during pregnancy. In addition, the results highlight the importance of considering bidirectional effects between maternal substance use and child behavior problems, and results are supportive of transactional theories of development. Finally, the results also add to the growing literature on sex differences in tobacco and cannabis exposure, and indicate generally stronger exposure effects for girls. In addition to these strengths, the study also has some limitations. One major limitation is that both maternal postnatal cannabis use and child behavior problems were measured using maternal reports. This raises the possibility that the bidirectional associations with cannabis exposure may be due, in part, to shared method variance. In addition, we were constrained by sample size from examining more complex models that included change over time from earlier waves and aspects of maternal psychopathology, such as depression and anger/hostility. Future studies with large sample sizes could examine potential bidirectional associations over longer periods of development. Finally, given the study design of recruiting tobacco smokers, the results cannot speak to potential independent prenatal cannabis effects. It is possible that the results could be explained by genetic or epigenetic influences. Our research design and measurement did not allow examination of these mechanisms. In spite of these limitations, this study adds to the sparse literature on co-occurring tobacco and cannabis exposure effects, sex differences in pre-and-postnatal exposure effects, and bidirectional associations between parent and child behaviors in early childhood.

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Highlights

- Tobacco exposed girls had more behavior problems compared to non-exposed girls.
- There were no differences among boys.
- There were dose-response effects of prenatal tobacco exposure.
- Behavior problems and mothers' postnatal cannabis use were predictive of each other.

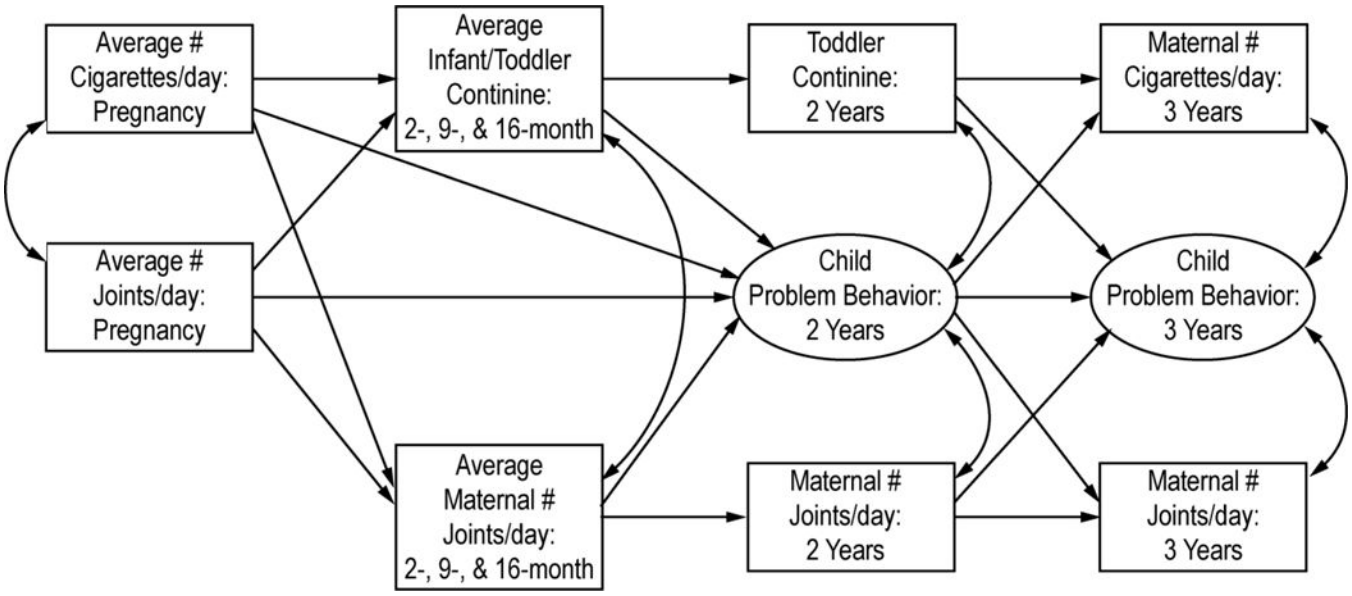

Figure 1.
Conceptual model.
Note. Residual covariances between postnatal tobacco and cannabis exposure at 2 and 3 years are not depicted in the figure but were included in the model.

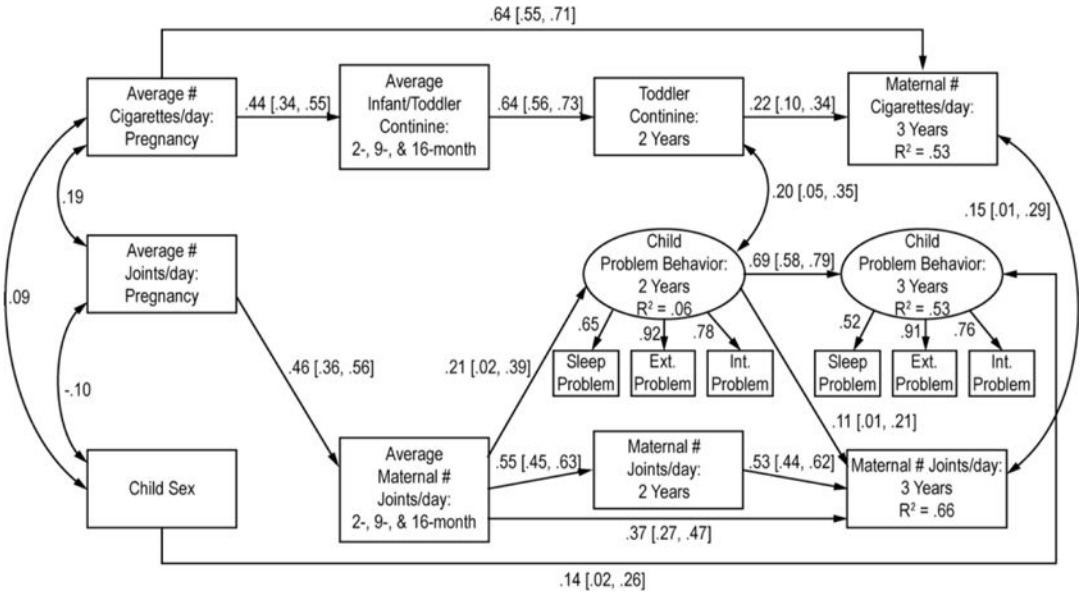

Figure 2.

Estimated structural model. Only statistically significant standardized parameters and 95% confident intervals(in brackets) are presented in the figure for ease of presentation. The full model included all of the covariances among the exogenous variables, the covariance between the postnatal substance use variables assessed within the same time point, the covariance between child problem behaviors and substance use within time, and paths from the exogenous variables to child outcomes. Thus, estimates related to maternal breastfeeding duration was not inlcuded since they were not significant. Continuous measures of maternal substance use were used for the prenatal variables. However, when two dummy-coded exposure variables reflecting group status with the control group as the comparison were used in model estimation, the results were similar. Ext: Externalizing, Int: Internalizing.

Table 1

Exposure Group Differences in Demographic Variables and Substance Exposure by Child Sex

	Non-smoking		Tobacco only		Tobacco & cannabis		F/χ^2	Partial η^2
	***M*/%**	***SD***	***M*/%**	***SD***	***M*/%**	***SD***		
			GIRLS					
Demographics								
Days of breast feeding during infancy	98.03[b] 24.31	152.91 5.57	28.29[a] 24.43	42.58 4.51	39.65[a] 23.45	88.31 4.33	**4.39** * .52	.07 * .01
Maternal age								
Maternal years of education	12.69	1.92	12.43	2.06	12.24	1.99	.56	.01
Maternal occupation	2.22	1.78	2.32	1.95	1.73	1.15	1.70	.03
Parity	1.83	1.24	1.91	1.77	1.63	1.73	.23	.01
Race (% White)	22.2%		25.0%		33.3%		χ^2 =1.44	
TANF	16.6%		21.4%		9.8%		χ^2 =2.09	
Medicaid	66.7%		64.3%		68.6%		χ^2 = .16	
Food stamps	52.8%		57.1%		56.8%		χ^2 = .18	
Partner smoking	44.4%		55.6%		90.0%		**χ^2 =9.44** **	
Prenatal exposure								
#Joints/Day Trimester 1	.00	.00	.00	.00	1.49	2.07		
#Joints/Day Trimester 2	.00	.00	.00	.00	.32	.76		
#Joints/Day Trimester 3	.00	.00	.00	.00	.15	.52		
#Cigarettes/Day Trimester 1	.00	.00	4.97	4.24	8.18	6.21		
#Cigarettes/Day Trimester 2	.00	.00	1.60	2.04	4.39	4.52		
#Cigarettes/Day Trimester 3	.00	.00	1.61	2.35	4.24	5.58		
#Drinks/Day Trimester 1	.04	.13	.10	.30	.34	.92		
#Drinks/Day Trimester 2	.00	.01	.00	.01	.00	.01		
#Drinks/Day Trimester 3	.00	.03	.00	.00	.00	.01		
Postnatal exposure								
# Joints/day (average 2, 9, &16 months)	.04[a]	.16	.08[a] .33		1.68[b]	2.93	**7.88** **	.15

	Non-smoking		Tobacco only		Tobacco & cannabis		F/χ^2	Partial η^2
	M/%	*SD*	*M*/%	*SD*	*M*/%	*SD*		
Average # joints/day 2 years	.02**a**	.11	.00[a] .00		.69[b]	.98	**12.42** ***	.22
Average # joints/day 3 years	.00[a]	.01	.00[a] .01		.43[b]	.89	**5.85** **	.12
Infant cotinine (average 2, 9, &16 months)	1.79[a]	1.46	6.15[b] 6.05		7.42[b]	5.76	**12.54** ***	.24
Infant cotinine 2 years	1.52[a]	2.05	4.07[b] 3.59		5.50[b]	4.69	**9.76** ***	.20
Average # Cigarettes/Day 3 years	.27[a]	1.48	5.93[b] 5.09		7.60[b]	6.16	**20.90** ***	.35
# Drinks/day (average 2, 9, &16 months)	.04[a]	.08	.12[a]	.21	.19[b]	.32	**4.06** *	.27
Average # drinks/day 2 years	.08	.20	.20	.29	.41	1.33	1.44	.03
Average # drinks/day 3 years	.04[a]	.67	.14[a]	.24	.66[b]	1.51	**4.01** *	.08
			BOYS					
Demographics								
Days of breast feeding during infancy	49.73 22.52	105.35 4.24	48.60 25.15	95.61 5.55	4 3.98 24.22	105.28 5.23	.0 4 2.67	.00 .04
Maternal age								
Maternal years of education	12.39	1.89	12.15	1.72	12.22	1.82	.18	.00
Maternal occupation	2.00	1.48	2.19	1.73	2.20	1.67	.17	.00
Parity	1.20	1.87	1.76	1.54	1.27	1.63	1.22	.02
Race (% White)	12.1%		51.0%		30.4%		**χ^2 =13.88** **	
TANF	9.1%		9.6%		21.7%		χ^2 = 3.83	
Medicaid	63.6%		65.4%		69.6%		χ^2 = .34	
Food stamps	51.5%		50.0%		56.5%		χ^2 = .44	
Partner smoking	36.8%		81.8%		93.8%		**χ^2 =15.76** ***	
Prenatal exposure								
#Joints/Day Trimester 1	.00	.00	.00	.00	.65	.94		
#Joints/Day Trimester 2	.00	.00	.00	.00	.21	.43		
#Joints/Day Trimester 3	.00	.00	.00	.00	.21	.43		
#Cigarettes/Day Trimester 1	.00	.00	7.50	6.42	7.96	5.31		

	Non-smoking		Tobacco only		Tobacco & cannabis		F/χ^2	Partial η^2
	M/%	*SD*	*M*/%	*SD*	*M*/%	*SD*		
#Cigarettes/Day Trimester 2	.00	.00	4.36	4.98	4.15	4.08		
#Cigarettes/Day Trimester 3	.00	.00	3.57	4.59	4.41	6.01		
#Drinks/Day Trimester 1	.03	.05	.17	.29	.22	.49		
#Drinks/Day Trimester 2	.00	.00	.00	.01	.01	.02		
#Drinks/Day Trimester 3	.00	.01	.00	.01	.01	.03		
Postnatal exposure								
# joints/day (average 2, 9, &16 months)	.01[a]	.02	.00[a]	.01	2.84[b]	5.66	**8.40*****	.15
Average # joints/day 2 years	.00[a]	.01	.00[a]	.01	.99[b]	1.62	**10.48*****	.20
Average # joints/day 3 years	.00[a]	.01	.03[a]	.16	.82[b]	1.77	**6.84****	.12
Infant cotinine (average 2, 9, &16 months)	2.25[a]	1.90	6.01[b]	7.50	8.65[b]	7.19	**7.31****	.14
Toddler cotinine 2 years	1.88[a]	3.34	3.37[b]	4.03	4.78[b]	4.63	**3.59***	.08
Average # Cigarettes/Day 3 years	1.17[a]	4.09	4.68[b]	5.29	6.92[b]	6.21	**8.31*****	.16
# Drinks/day (average 2, 9, &16 months)	.04	.07	.19	.37	.29	.65	2.95	.04
Average # drinks/day 2 years	.15	.69	.21	.53	.27	.44	.44	.01
Average # drinks/day 3 years	.05[a]	.09	.14[a]	.24	.29[b]	.46	**4.67***	.09

Note. TANF: Temporary Assistance to Needy Families.

Means with different superscripts were significantly different from each other.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 2

Exposure Group Differences in CBCL Problem Behaviors by Child Sex

	Non-smoking		Tobacco only		Tobacco & cannabis		*F* value	Partial η^2
	M	***SD***	***M***	***SD***	***M***	***SD***		
				GIRLS				
CBCL subscales (3 years)								
Emotionally reactive	1.79[a]	1.83	2.67[b]	1.80	1.49[a]	1.43	**3.83** *	.08
Anxious/depressed	1.39[a]	2.29	2.81[b]	2.14	1.90[a]	1.91	**3.65** *	.07
Somatic complaints	1.94	1.33	1.33	1.15	.73	1.07	2.05	.04
Withdrawn	1.00[a]	1.80	1.95[b]	2.16	.46[a]	.78	**7.05** **	.13
Internalizing problems	5.12[a]	5.06	8.76[b]	5.44	4.59[a]	3.41	**6.58** **	.13
Attention problems	1.76[a]	1.83	3.05[b]	1.72	2.07[ab]	1.59	**4.02** *	.08
Aggressive behavior	7.91	8.64	11.10	6.70	9.33	5.17	1.84	.04
Externalizing problems	9.67	10.04	14.16	7.48	11.34	6.27	2.50	.05
Sleep problems	2.06[a]	2.21	3.95[b]	2.84	2.73[ab]	2.38	**4.19** *	.08
				BOYS				
CBCL subscales (3 years)								
Emotionally reactive	2.01	1.83	1.83	1.87	1.67	1.79	.26	.01
Anxious/depressed	2.37	2.29	2.21	2.23	1.86	1.80	.50	.01
Somatic complaints	1.33	1.33	1.27	1.34	1.49	1.44	.26	.01
Withdrawn	1.49	1.80	1.19	1.80	1.54	1.58	.46	.01
Internalizing problems	6.96	5.06	6.46	5.77	6.45	4.76	.09	.00
Attention problems	2.44	1.83	2.55	1.76	2.60	1.97	.06	.00
Aggressive behavior	11.44	8.64	10.10	6.45	9.70	6.14	.51	.01
Externalizing problems	13.89	10.04	12.64	7.73	12.30	7.75	.29	.01
Sleep problems	2.78	2.21	3.07	2.38	3.29	2.76	.32	.00

Note. Means with different superscripts were significantly different from each other.

* $p < .05$.

** $p < .01$.

Table 3

Correlations between Prenatal Substance Exposure (Dosage) and CBCL Problem Behaviors for Girls and Boys

	CBCL subscales (3 years)								
	ER (α = .72)	**AD (α = .66)**	**SC (α = .33)**	**W (α = .68)**	**INT**	**AP (α = .62)**	**AG (α = .90)**	**EXT**	**SL**
				GIRLS					
Maternal self-reports									
#Cigarettes/Day Trimester 1	−.03	**.29****	−.01	.01	.11	.12	.17	.16	.11
#Cigarettes/Day Trimester 2	−.07	**.23***	−.02	−.07	.05	−.01	.06	.05	.01
#Cigarettes/Day Trimester 3	−.06	**.33****	−.06	−.01	.10	.01	.03	.03	.03
#Cigarettes/Day Pregnancy	−.05	**.31****	−.03	−.02	.10	.06	.12	.11	.07
#Joints/Day Trimester 1	−.20	−.05	−.16	−.17	−.18	−.18	.07	.01	−.01
#Joints/Day Trimester 2	−.15	.00	−.19	−.11	−.14	−.13	−.01	−.04	−.11
#Joints/Day Trimester 3	−.07	.08	−.10	−.05	−.03	−.13	−.13	−.14	−.13
#Joints/Day Pregnancy	−.20	−.03	−.16	−.15	−.17	−.19	.04	−.02	−.05
Meconium									
Cotinine	−.01	−.07	−.18	−.20	−.13	−.20	.04	−.02	−.04
Cannabis	−.22	−.02	**−.28***	−.16	−.19	−.21	−.13	−.15	−.12
				BOYS					
Maternal self-reports									
#Cigarettes/Day Trimester 1	.01	.04	.02	.04	.03	**.23***	.03	.08	.11
#Cigarettes/Day Trimester 2	−.06	.01	.02	.01	.00	.19	−.01	.04	.06
#Cigarettes/Day Trimester 3	−.04	−.02	−.03	−.03	−.01	**.23***	.01	.06	.04
#Cigarettes/Day Pregnancy	−.01	.01	.03	.01	.02	**.23***	.02	.06	.08
#Joints/Day Trimester 1	.03	.02	.14	.07	.08	−.04	−.01	−.02	.11
#Joints/Day Trimester 2	−.08	−.09	.01	.01	−.06	−.14	−.08	−.10	−.03
#Joints/Day Trimester 3	−.10	−.11	−.07	.10	−.07	−.05	−.02	−.03	−.03
#Joints/Day Pregnancy	.01	.00	.12	.07	.05	−.06	−.02	−.03	.09
Meconium									
Cotinine	−.11	−.13	.06	−.06	−.07	.02	−.03	−.02	.12
Cannabis	.05	.01	.14	.15	.10	.06	.03	.03	−.03

Note. ER = emotionally reactive; AD = anxious/depressed; SC = somatic complaints; W = withdrawn; INT = internalizing; AP = attention problems; AG = aggressive behavior; EXT = externalizing; SL = sleep problems.

* $p < .05$.

** $p < .01$.

Table 4

First-Order Correlations among Postnatal Substance Exposure and Child CBCL Problem Behaviors.

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	CBCL (2 years)																								
1	Sleep problems	---	.55**	.51**	.48**	.46**	.42**	.30**	.43**	.53**	.53**	.33**	.26	.13	.18	.42**	.12	.38**	.30**	−.03	−.04	.05	−.03	.07	.00
2	Externalizing problems	.59**	---	.72**	.67**	.66**	.40**	.45**	.75**	.98**	.33**	.61**	.46**	.46**	.32**	.33**	.40**	.50*	.59*	.03	.02	.10	−.15	.11	.01
3	Internalizing problems	.56**	.70**	---	.82**	.85**	.67**	.76**	.58**	.70**	.23**	.57**	.60**	.47**	.46**	.41**	.56**	.45**	.56**	−.01	−.03	.01	−.11	.04	.14
4	Emotionally reactive	.52**	.68**	.87**	---	.70**	.44**	.44**	.45**	.67**	.28**	.38**	.30**	.60**	.43**	.29**	.42**	.43**	.57**	−.09	−.09	−.08	−.15	−.02	−.18
5	Anxious/depressed	.50**	.70**	.89**	.78**	---	.44**	.48**	.56**	.63**	.11	.33**	.32**	.42**	.44**	.35**	.49**	.47**	.49**	.01	−.09	−.03	−.02	.08	−.05
6	Somatic complaints	.48**	.25**	.59**	.35**	.36**	---	.55**	.33**	.39**	.06	.01	.24**	.11	.19	.45**	.22*	.23*	.25*	.04	.08	.17	.02	.09	−.08
7	Withdrawn	.30**	.46**	.77**	.54**	.57**	.32**	---	.40**	.43**	.05	.15	.16	.29**	.36**	.36**	.58*	.25*	.41*	−.02	−.03	.01	−.05	.05	−.14
8	Attention problems	.50**	.85**	.59**	.56**	.57**	.26*	.39**	---	.61**	.22**	.47**	.44**	.25*	.22*	.25*	.34*	.46*	.28*	.02	.01	.08	−.17	.09	.02
9	Aggressive behavior	.58**	.99**	.69**	.68**	.70**	.23**	.45**	.76**	---	.27*	.51**	.25*	.48**	.32**	.32**	.37**	.47**	.63**	.03	.02	.10	−.13	.11	−.02
	CBCL (3 years)																								
10	Sleep problems	.46**	.27*	.18	.28*	.16	.06	.05	.22*	.27*	---	.41**	.39**	.31**	.27**	.47**	.27**	.35**	.40**	.17	.04	.13	.08	.10	.05
11	Externalizing problems	.31**	.53**	.31**	.38**	.33**	.01	.15	.47**	.51**	.49**	---	.73**	.75**	.63**	.42**	.53**	.80**	.99**	.23	−.02	.15	−.07	.10	.02
12	Internalizing problems	.27**	.30**	.36**	.30*	.32**	.24*	.16	.41**	.25*	.46*	.62**	---	.78**	.88**	.69**	.78**	.53**	.73**	.24	.04	.19	−.08	.11	.05
13	Emotionally reactive	.31*	.37**	.41*	.52**	.39**	.16	.13	.35**	.35**	.49*	.56**	.74**	---	.63**	.36**	.47**	.57**	.75**	.24*	.05	.20*	−.10	.01	−.08
14	Anxious/depressed	.08	.20	.22*	.16	.26*	.10	.08	.31**	.16	.22*	.47**	.82**	.40**	---	.52**	.60**	.44**	.64**	.25*	−.02	.14	−.05	.16	−.08
15	Somatic complaints	.35**	.19	.20	.08	.14	.43**	.07	.27*	.11	.41**	.25*	.60**	.34**	.34**	---	.44**	.26*	.44**	.29*	.14	.27**	−.09	.10	.04
16	Withdrawn	.13	.11	.20	.09	.19	.11	.29**	.28*	.05	30**	.50**	.78**	.44**	.54**	.30**	---	.42**	.52**	.12	−.02	.07	−.02	.08	.08
17	Attention problems	.35**	.44**	.21	.17	.16	.12	.11	.50**	.40**	.43**	.80**	.54**	.41**	.38**	.36**	.46**	---	.70**	.21*	.00	.16	.00	.18	.11
18	Aggressive behavior	.28*	.52**	.32*	.42**	.35**	.05	.15	.44**	.51**	.48*	.99**	.59**	.57**	.50**	.20	.47**	.68**	---	.22*	−.03	.14	−.09	.07	−.03
	Postnatal substance exposure																								
19	Maternal # joints/day (average 2, 9, & 16 months)	−.05	.04	.10	.13	.17	−.13	.20	.02	.08	−.03	−.07	−.12	−.10	.01	−.13	−.10	−.13	.00	---	.59**	.79**	.06	.19*	.06
20	Average maternal # joints/day 24 months	−.11	.01	−.02	.06	.02	−.07	.04	.00	.04	−.05	−.09	−.10	−.08	.10	−.13	−.14	−.11	−.03	.48**	---	.76**	.22*	.10	.11
21	Average maternal # joints/day 36 months	−.07	.12	.18	.20	.19	−.08	.30**	.05	.17	−.08	−.10	−.12	−.09	.04	−.14	−.10	−.13	−.04	.45**	.81**	---	.04	.09	.13
22	Infant cotinine (average 2, 9, & 16 months)	.23*	.30**	.15	.18	.14	.06	.15	.23*	.40**	.16	.15	.08	.12	.11	.05	−.05	.19	.12	.04	.17	.06	---	.57**	.36**

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
23	Toddler cotinine 24 months	.14	.20	.13	.13	.12	.02	.17	.19	.19	.18	**.22** *	.19	.10	**.28** *	.08	.01	**.27** *	.19	.05	.13	.09	**.67** **	---	**.37** **
24	Maternal # Cigarettes/Day 36 months	−.05	.09	−.03	.07	.03	−.16	−.10	.01	.09	.13	.05	.11	.12	**.25** *	−.01	−.10	.04	.03	.17	**.47** **	**.37** **	**.51** **	**.56** **	---

Note. Correlation matrixes above and below the broken diagonal line were for boys and for girls, respectively.

* $p < .05$.

** $p < .01$.