



## Full length article

## 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.

**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.

## 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

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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; Wiebe 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 et al., 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 et al., 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

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