Is Smoking During Pregnancy a Risk Factor for Psychopathology in Young Children? A Methodological Caveat and Report on Preschoolers

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Objective While studies of the effects of prenatal smoking on child psychopathology have found positive relationships, most studies (1) failed to control for a range of correlates of maternal smoking that could affect children’s behavior; (2) have been conducted with school-age rather than younger children, so it is not clear when such problems emerge; and (3) have not examined the effects on internalizing problems.

Method This study examined the effects of prenatal smoke exposure on behaviors associated with externalizing and internalizing behavior problems and negative temperament in a diverse community sample of 679 4-year-olds.

Results After controlling for correlates that include socioeconomic status, life stress, family conflict, maternal depression, maternal scaffolding skills, mother–child attachment, child negative affect and effortful control, smoking during pregnancy was no longer associated with child behavior or emotional problems.

Conclusions Future studies need to control for a wide range of covariates of maternal smoking.

Key words adjustment; mental health; parenting; risk; smoking.

Introduction Cigarette smoking has harmful effects on the fetus, leading to premature differentiation of developing neural tissue, altered noradrenergic and dopaminergic central nervous system pathways (van Ijzendoorn, Vereijken, Bakermans-Kranenburg, & Riksen-Walraven, 2004), and intrauterine growth retardation (Lassen & Oei, 1998). Many studies suggest that smoking during pregnancy is a risk factor affecting the development of externalizing behavior problems via the neurological or physiological changes that smoking produces in utero. The resulting externalizing problems may include oppositional or antisocial behavior (Wakschlag, Pickett, Cook, Benowitz, & Leventhal, 2002), Attention Deficit Hyperactivity Disorder (Linnell et al., 2003), or both.

Demonstrating a direct association between smoking during pregnancy and behavior problems is complicated by the presence of confounding risk factors that provide alternative explanations for any smoking/behavior problem relationship (Wakschlag et al., 2002). Because mothers who smoke during pregnancy differ on important variables from those who do not (Button, Maughan, & McGuffin, 2007; Wakschlag et al., 2002) and random assignment to prenatal smoking conditions is not possible, statistical
procedures must control for demographic, physical and psychosocial factors during pregnancy or early childhood that co-occur with smoking during pregnancy and that can be associated with child behavior problems. Nevertheless, residual effects of covariates may still remain after statistical controls are applied (Wakschlag et al., 2002). Eliminating any residual effects after applying statistical controls and controlling for every conceivable correlate of maternal smoking may be impossible, but confidence in the findings of such studies will increase if the range of covariates examined is reasonably comprehensive.

Viewed from another perspective, failure to include critical psychosocial variables when studying the effects of smoking during pregnancy may result in an “omitted variables” problem, in which the effect of a particular risk variable is over-estimated when constructs playing a role in the causal structure of the outcome variable are omitted from analysis. The “omitted variables” problem is considerable in studies of the etiology of psychopathology (Tomarken & Waller, 2003), biasing estimates of causal parameters in the model or leading to inaccurate standard errors affecting significance levels of relationships. It is even possible for an omitted variable to completely account for the effects of a variable included in the model (Tomarken & Waller, 2003). While an emphasis on “controlling for” certain variables might lead researchers to be satisfied with including variables known to correlate with smoking during pregnancy, attending to omitted variables emphasizes inclusion of a wider range of variables associated with the outcome measure in order to obtain a more accurate estimate of the magnitude of the effects of smoking during pregnancy on child psychopathology.

**Psychosocial Correlates of Smoking During Pregnancy**

Wakschlag et al. (2002) noted that pregnant women who smoke differ from nonsmokers in several ways, including contextual factors, presence of psychiatric disorder, and parenting behavior. Variables studied along with smoking during pregnancy vary widely across studies in the literature; these may include contextual factors (i.e., demographics, such as maternal education, socioeconomic status) parental psychological problems (e.g., conduct disorder, depression), parenting variables (e.g., warmth, hostility), family climate factors (e.g., stressors, conflict in the home) and child health factors (e.g., birth weight, other illnesses). Few studies, however, include covariates from each of these categories. Controlling for demographic factors usually occurs (Ashford, van Lier, Timmermans, Cuijpers, & Koot, 2008; Batstra, Hadders-Algra, & Neeleman, 2003; D’Onofrio et al., 2008) but not always (Brennan, Grekin, & Mednick, 1999; Silberg et al., 2003), while pre- and perinatal factors, including birth weight, are often (Cornelius, Ryan, Day, Goldschmidt, & Willford, 2001; Weitzman, Gortmaker, & Sobol, 1992), but not always (Brook, Brook, & Whiteman, 2000; Linnett et al., 2003), included as covariates. Similarly, attention to psychosocial factors is inconsistent. Controlling for parental psychopathology is relatively common, but few studies have assessed family conflict and life stress, or attempted to assess parenting attitudes, behavior, and the family environment. Although several studies have found a relationship between smoking during pregnancy and behavior problems after controlling for maternal hostility and supportive home environment, other important aspects of parenting and the parent–child relationship (e.g., attachment security) have been overlooked. D’Onofrio et al. (2008) argue that important, yet unidentified, environmental factors may account for the relationship between smoking during pregnancy and externalizing behaviors, including Attention Deficit Hyperactivity Disorder (ADHD). Identifying and examining the effects of such variables is important if an unbiased estimate of the effects of smoking during pregnancy is to be obtained.

**Genetic Factors**

Recently, the possibility of genetic factors confounding the study of the effects of smoking during pregnancy on child behavior outcomes has been raised (Knopik, 2009). Genetic confounding can occur, for example, if mothers with ADHD who are more likely to smoke also transmit genes that predispose the child to developing ADHD. To address genetic confounds, genetically-sensitive designs are needed to estimate the relative contributions of genetic factors and smoking during pregnancy. Such studies are still uncommon. D’Onofrio et al. (2008) used a genetically informed design to study the effects of smoking during pregnancy on externalizing disorders. This study included mothers and their children, ages 4–10 years, from the National Longitudinal Survey of Youth. The study is “genetically informed” because data on various kinship pairs, including twins, full siblings, half-siblings, and cousins, among others, were collected and used to estimate the genetic effects contributing to the relationship between smoking during pregnancy and child problems. The authors concluded that: (1) smoking during pregnancy was not associated with conduct or oppositional behavior problems; (2) there was a small relationship between smoking during pregnancy and attention deficit symptoms, with the relationship reduced by methodological and statistical controls; and (3) the confounds were less likely to be genetic than environmental. However, the maternal
“environmental” characteristics examined only included intellectual ability, education, income, delinquency, and age at delivery, which have not been shown to be significant psychosocial confounds in the extant literature on the relationship between prenatal smoking and behavior problems. Knopik et al. (2006) used a children-of-twins design to study genetic factors associated with ADHD and prenatal alcohol use and smoking on ADHD. In such a design, the children vary in prenatal exposure to alcohol and smoking depending on maternal use, and also on genetic risk. The Knopik et al. study was primarily concerned with alcohol use during pregnancy, but smoking during pregnancy was highly correlated with prenatal alcohol use. The results suggest that genetic transmission plays an important role in the association between maternal alcohol use and offspring ADHD, with prenatal exposure to smoking increasing the risk for ADHD. This children-of-twins design and other promising genetic approaches may improve our ability to obtain an unbiased estimate of the effect of smoking during pregnancy on behavior problems in future studies (Knopik, 2009). Such designs include molecular genetic approaches examining specific target genes; co-twin control designs that include twin pairs differing on the outcome of interest, or some other environmental factor (Knopik, 2009); or even prenatal cross-fostering designs comparing mothers who are either biologically related or unrelated to the child after undergoing in vitro fertilization (Rice et al., 2009).

**Studying Causal Mechanisms versus Reducing Confounds**

In the field of developmental psychopathology, increasing attention is being devoted to studying the causal mechanisms underlying the relationships between purported risk factors and outcomes. Many researchers are interested in the process of mediation, in which an independent variable is thought to affect a dependent variable through some intervening variable known as a mediator (Iacobucci, 2008). With the exception of the Nigg and Breslau (2007) study discussed later, researchers have not posited that psychosocial variables serve as mediators of the relationship between smoking during pregnancy and child behavior problems. Causal modeling must begin with a strong, coherent theoretical rationale, and thus far no researchers have posited that smoking during pregnancy leads to a parent having lower socioeconomic status (SES), more conflict at home, or poor parenting. Thus, such psychosocial factors are viewed as smoking correlates, possibly related to an underlying “third variable,” rather than as mediators of the prenatal smoking/child behavior relationship. As a result, these studies have not typically examined mediation; rather, statistical procedures attempt to control for the effects of these correlates so that the specific effect of smoking during pregnancy on behavior problems can be assessed.

**Studies of Young Children**

A second problem in the literature on smoking during pregnancy is the absence of studies of young children that address the omitted variables problem and, thereby, rule out alternative explanations of the data by including a wide range of risk variables in the causal model. Studies of young children are important: identifying a relationship between smoking during pregnancy and psychopathology in preschoolers can point to the early onset of the relationship between this prenatal risk factor and problem behaviors, while the absence of such a relationship may suggest a mediating role for environmental risk factors or child characteristics that become important as children enter school or transition to adolescence. Studies of preschoolers can help further our understanding of the developmental progression of the linkage between smoking during pregnancy and psychopathology.

Among studies of smoking during pregnancy and ADHD in young children, only one attempted to control concurrently for demographic factors, family environment, parental psychopathology, parenting, and prenatal factors. Romano Tremblay, Farhat, & Cote (2008) found that smoking during pregnancy was associated with ADHD symptoms in 2- to 7-year-olds, while controlling for SES, maternal depression, family dysfunction and maternally reported parental warmth and hostility. That study, however, was limited by its use of a three-item ADHD scale with unreported psychometric properties. Other investigators studying the relationship between smoking during pregnancy and ADHD symptoms in predominantly preschool samples have failed to control for parenting and family environmental effects (Streissguth, Martin, Barr, & Sandman, 1984), parental psychopathology (Huijbregts et al., 2007; McGee & Stanton, 1994) or family climate, including stress or conflict (Huijbregts et al., 2007).

Among studies of the effects of smoking during pregnancy on externalizing disorders in young children, only two studies controlled for at least one covariate in each area of demographic, parental psychopathology, parenting, environment, family stress, and pre-or perinatal factors. Results from one of these studies (Day, Richardson, Goldschmidt, & Cornelius, 2000) suggest a relationship between smoking during pregnancy and inattention, and results from the other (Walschlag, Levental, Pine, Pickett, & Carter, 2006) suggest a relationship between smoking during pregnancy and externalizing problems at
24 months. The latter study was limited by a lack of racial/ethnic diversity in the sample. Other studies finding a relationship between smoking during pregnancy and externalizing problems in preschoolers failed to control for family climate and parenting factors such as parental warmth (Williams et al., 1998), perinatal factors or parental psychopathology (Huijbregts et al., 2007), or multiple types of parenting or psychosocial factors (O’Callaghan, Williams, Andersen, Bor, & Nahman, 1997; Orlebeke, Knol, & Verhulst, 1997; Stene-Larsen & Borge, 2009; Wakschlag & Keenan, 2001).

Furthermore, Nigg and Breslau (2007) posit an important role for temperament in young children as a mediator of the relationship between smoking during pregnancy and subsequent externalizing problems. Nigg and Breslau proposed a model in which: (1) prenatal smoke exposure “amplifies” irritable temperament in children; and (2) this “lays the foundation for negative parent–child interchanges” that can generate oppositional defiant disorder (ODD) symptoms. The model implies certain testable hypotheses, including: (a) preschool children exposed to smoking \textit{in utero} are more likely to have a difficult or “irritable” temperament; (b) the effects of smoking during pregnancy on the development of ODD symptoms are mediated by negative temperament. A study by Brook et al. (2000), in which smoking during pregnancy was associated with temperament. A study by Brook et al. (2000), in which smoking during pregnancy was associated with temperament. A study by Brook et al. (2000), in which smoking during pregnancy was associated with temperament.

**Internalizing Disorders**

Another limitation in the literature on smoking during pregnancy is the lack of attention to internalizing disorders. Since nicotine exposure affects the norepinephrine and serotonin neurotransmitter systems associated with anxiety and depression (Ashford et al., 2008), the impact of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study. We have identified only three studies of the effects of smoking during pregnancy on internalizing problems merits further study.

**The Present Study**

The present study examines whether there is a direct effect of smoking during pregnancy on child psychopathology, addressing several of the methodological limitations in the literature in several ways. First, this study extends the limited range of studies of smoking during pregnancy and children’s behavior problems in preschool children by examining its effects in 4-year-olds. Second, we examined the effects of smoking during pregnancy on internalizing, as well as externalizing and attentional, problems.

Third, we included a wider range of psychosocial covariates than has previously been examined. The present report is based upon data collected during the first wave of a longitudinal study of the risk factors and correlates of the development of oppositional behavior, anxiety, and depression in young children. We selected the risk factors to be studied based on Bronfenbrenner’s (1979) bioecological model, Cicchetti and Toth’s (1998) transactional model of childhood depression, and Campbell’s (1990) model of the development of externalizing behaviors. We also reviewed the literature associated with the development of these disorders to identify additional, specific risk factors that had been studied but not noted in the general models. As Smeekens, Riksen-Walrave, and van Bakel (2007) have noted, there are four domains of variables that have generally been proposed to be related to the development of child externalizing problems; given the relative absence of studies of specificity of risk factors (Shanahan, Copeland, Costello, & Angold, 2008) and prior literature, the domains appear to be relevant to internalizing disorders, as well. These domains include: (1) contextual characteristics (e.g., SES, stress); (2) parental characteristics (e.g., personality, psychopathology); (3) parenting (e.g., support, scaffolding, hostility); and (4) child characteristics (e.g., attachment, temperament). We included risk factors from each of these domains as possible psychosocial covariates of smoking during pregnancy.

Fourth, the present study used multiple outcome measures rather than relying on single measures, as in most prior studies. Finally, the present study examined the role that NA may play as a preschool-age precursor to the development of later problem behaviors as proposed by Nigg and Breslau (2007).

Although the present study offers some methodological advantages over prior studies, noted above, it is limited by its use of retrospective report of smoking. As Knopick (2009) has noted, there are times when a retrospective report on smoking during pregnancy is necessary, even though prospective reports, particularly those accompanied by obtaining serum cotinine levels from the mother, are ideal. Since the present study was initiated when the children were 4 years old, retrospective reports were necessary. The use of retrospective reports in the literature on smoking during pregnancy, however, is not uncommon.
and collecting serum cotinine levels is still quite unusual. In addition, while studying 4-year-olds means that behavior problems that emerge early in the child’s life could be studied, problems that might emerge later in life could not be examined in the present report.

Methods

Participants

Participants were part of the first wave of the longitudinal study described above. Children were recruited from 23 primary care pediatric practices throughout Cook County, Illinois, and at 13 Chicago Public Schools with preschool programs.

At the time of initial contact at the schools and practices, 1738 families expressed an interest in learning more about the study. Subsequently, these families were contacted by telephone to provide them with additional information, and 831 (47.8%) families then completed the Wave 1 evaluation. That participation rate was similar to that in one prior preschoolers’ study (Lavigne et al., 1993); it could not be compared to those of other large community studies of children in this age group (Egger & Angold, 2006) because the recruitment rates were not described in those reports. There were 35 children who did not meet the following inclusion criteria: (1) child did not exhibit an autistic spectrum disorder; (2) child and parent spoke Spanish or English; (3) child had lived with the same primary caretaker for the prior 6 months (because otherwise the caretaker may not have had sufficient experience to report on the child’s functioning); (4) child obtained a standard score on a language screen above 70 at baseline, was not enrolled in a classroom for the mentally retarded, or did not have a school IQ test below 70. because he/she would not be able to participate in certain study tasks. Data on smoking during pregnancy were not provided for an additional 117 families, including 30 families in which fathers completed study questionnaires. Because smoking during pregnancy may be related to race or ethnicity, we restricted the sample to the three largest race/ethnicity groups in the sample (non-Hispanic whites, \( n = 421 \), 62.0%; African Americans, \( n = 113 \), 16.6%; Hispanic Whites, \( n = 145 \), 21.4%). Thus, the final sample for analysis of the effects of smoking during pregnancy consisted of 679 children and families. The sample included 338 boys (49.8%) and 341 girls (50.2%). The mean age was 4.43 years (range 3.87–5.14 years) at the time of assessment. While all SES groups were represented, the sample was skewed in the direction of the higher two Hollingshead SES groups (74.4% higher in two SES groups). Smoking during pregnancy occurred in 7.5% (\( n = 51 \)) of the sample.

Measures

Demographics

Mothers completed a demographic questionnaire that provided information concerning education and employment to be coded into the Hollingshead Four-Factor Index of Social Status (Hollingshead, 1975).

Smoking during Pregnancy

The measure of smoking during pregnancy from the Smoke-Free Families clinical trials (Melvin, Tucker, & Group, 2000) was used and information on smoking obtained at the first wave visit with the family. Women were asked: (a) if they had never smoked; (b) if they stopped smoking before becoming pregnant and no longer smoke; (c) stopped before pregnancy and resumed after the pregnancy; (d) if they continued to smoke after they became pregnant and no longer smoke; (e) if they continued to smoke after they became pregnant and were still smoking. Women were considered to have smoked during pregnancy if they reported they continued to smoke after they became pregnant (category d and e) regardless of current smoking status. Children were classified as exposed versus not exposed to smoke prenatally.

As noted above, prospective reports on smoking are preferable but, since prospective reports cannot always be obtained (Knopik, 2009), it is important to determine the accuracy of retrospective reports. Pregnancy is a time of high importance to most women, and recall of events during that time may differ from that for other periods. Indeed, studies suggest that long-term recall of events during pregnancy is generally quite good. In one report (Tomoe et al., 1999), women were contacted 30 years, on average, after their pregnancy and asked about specific pregnancy-related events. Their responses were compared to those obtained during their pregnancy as part of the National Collaborative Perinatal Project. Sensitivity of their recall of smoking was .86; specificity was .94. In a second study (Heath et al., 2003), the reliability of retrospective recall was assessed by comparing reports of women about smoking during pregnancy with those of their twin sisters. There was good agreement for self-report and informant (sister)-report of smoking during pregnancy.

While retrospective reports are never preferred, these data provide adequate support for the use of retrospective reports of the presence/absence of smoking during pregnancy.

Composite Measures of Risk Factors

As part of the longitudinal study design, multiple measures were used for several risk factors. To reduce the number of predictors and avoid multicollinearity in the present study,
composite measures of life stress, family conflict, maternal depression, and support/scaffolding were created by converting each measure to standard scores and calculating the sum of the standard scores to create composite measures.

Life Stress
A composite life stress measure was created from: (1) the total stress score of Abidin’s (1995) Parenting Stress Index Short Form, a measure with acceptable internal consistency (i.e., $\alpha$ values >0.9) and test–retest reliability coefficients between .65 and .96 (Lessenberry & Rehfeldt, 2004); (2) the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), a measure with high internal consistency ($\alpha = .84$) and test–retest reliability (.86), which correlates well with other measures of life stress; and (3) the McCubbin Family Changes & Strains Scale (McCubbin, Thompson, & McCubbin, 1996), $\alpha = .79$.

Family Conflict
A composite family conflict scale was created from: (1) the Family Environment Scale conflict scale (Moos & Moos, 1981); (2) the McCubbin Family Distress Index, a measure of family pressures and lack of social support ($\alpha = .87$) (McCubbin et al., 1996); and (3) the McCubbin Family Problem Solving/Communication scales (McCubbin et al., 1996), which assesses conflict-related family communication ($\alpha = .89$; test–retest reliability = .86).

Maternal Depression
A composite measure of maternal depression was created from: (a) the Beck Depression Inventory (Beck & Steer, 1987; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), with an average internal consistency ($\alpha = .86$) in clinical samples (Beck, Steer, & Garbin, 1988); (b) the Center for Epidemiological Studies-Depression Scale (Radloff, 1977), ($\alpha > .85$), moderate reliability (.45–.70 across several weeks), and validity as reflected in correlations with other depression scales (Radloff, 1977).

Maternal Support and Hostility
Maternal support and hostility were assessed with the Parent Behavior Inventory (Lovejoy, Weis, O’Hare, & Rubin, 1999). The two factor-analytically derived subscales, Support/Engagement and Hostility/Coercion have internal consistencies of .90 and .87 for the Support/Engagement and Hostility/Coercion scales, respectively. Test–retest reliabilities are .74 and .69, respectively.

Support/Scaffolding
A composite measure of parental support/scaffolding was created from the NICHD Three Boxes task (NICHD Early Childhood Research Network, 1999). This task consists of two activities that are designed to be too difficult for the child to accomplish without parental assistance, and a free-play, parent–child activity. Maternal behavior during the 15-min interaction is videotaped and rated on support/scaffolding ability, i.e., skills and affect suited for assisting a child in dealing with demanding tasks. Ratings are made on seven-point Likert scales on the following dimensions: supportive presence, quality of assistance, cognitive stimulation, respect for autonomy, maternal confidence, and hostility. Coders were trained to 80% reliability with two master coders, and a random sample of 20% of the tapes was double-coded to assess inter-rater reliability. Reliability ranged from .69 for maternal hostility to .80 for quality of assistance, with a mean reliability of .74. There was a low base rate of maternal hostility during the videotaped sessions which may have affected the intraclass correlations for this variable. The composite measure of scaffolding skills was calculated by summing the standard scores for supportive presence, respect for autonomy, cognitive stimulation, quality of assistance and confidence, and hostility (reverse coded).

Attachment
The Attachment Q-Sort (AQS) is a measure of attachment security suitable for use with preschoolers that utilizes Q-sort methodology to provide a continuous measure of attachment security (Waters, 1987). After the 2-h home visit that included a 45-min free interaction period as well as interaction during the mother–child interaction tasks, observers sorted 90 behavioral descriptions into nine piles according to similarity with the target child’s behavior. A security score was calculated by correlating the child’s sort with that of a prototypically secure child. A recent meta-analysis indicates that the AQS is a valid, reliable measure when using observer ratings (van IJzendoorn et al., 2004). Inter-rater reliability was assessed by randomly selecting (in blocks of 10) 20% of the home visits to be double-coded by two graduate research assistants. Inter-rater reliability was .77. Observers were blind to results for all other measures of child and family functioning.

Child Temperament: Negative Affect
The Children’s Behavior Questionnaire (CBQ) negative affectivity (NA) scale of the was used to assess NA (Rothbart, Ahadi, Hershy, & Fisher, 2001). Rothbart et al. (2001) define temperament as “constitutionally based individual differences in reactivity and self-regulation” (p. 1395). The NA scale combines parent ratings of the child’s!discomfort, fear, anger/frustration, and sadness, with soothability (negatively loaded). Item-total correlations for the CBQ range
from .64 to .92 for 4 year olds, and 2-year stability is .69 (Rothbart et al., 2001).

**Measures of Internalizing and Externalizing Symptoms**

Three measures assessed symptoms of ADHD (Diagnostic Interview Schedule for Children-Parent Scale-Young Child: DISC-YC; Child Symptom Inventory (CSI) ADHD scales; DuPaul ADHD Rating Scales), ODD (DISC-YC ODD scale, CSI ODD scale, Eyberg Scale), anxiety symptoms (DISC-YC generalized anxiety scale, CSI generalized anxiety scale and CSI separation anxiety scale) and depressive symptoms (DISC-YC major depression scale; CSI major depression scale, CSI dysthymia scale). For ADHD, the inattentive (ADHD-I), and hyperactive (ADHD-H) subtypes were examined separately, as well as the combined type (ADHD-C), because recent factor analysis suggests the two subtypes are well-differentiated in preschoolers (Sterba, Egger, & Angold, 2007).

**Diagnostic Interview Schedule for Children-Parent Scale—Young Child Version**

The young children’s Diagnostic Interview Schedule for Children-Parent Scale—Young Child Version (DISC-YC) (Fisher & Lucas, 2006) is a developmentally appropriate adaptation of the DISC-P, a DSM-IV-based structured parent interview. Because the rates of disorder were expected to be low in this sample, the symptom counts for each disorder were used rather than the presence versus absence of disorder. High levels of agreement are obtained for concrete, observable symptoms, and test–retest reliabilities for the DISC-YC are high. Overall reliability of symptom scales (C. Lucas, personal communication, 2006) is acceptable to high (test–retest reliability for ADHD scales = .67; for ODD, test–retest reliability = .88; for anxiety and depression scales = .57–.81). Ratings were obtained for ADHD symptoms (combined, inattentive and hyperactive/impulsive), ODD, anxiety and depression.

**CSI**

The parent form of the CSI (Gadow & Sprafkin, 1997, 2000) is a problem behavior checklist with items derived from DSM-IV diagnostic criteria. Each scale was treated as a continuous measure yielding T-scores. Overall reliability of symptom scales is acceptable to high for ADHD scales (α = .91; test–retest reliability = .67); ODD (α = .70; test–retest reliability = .90); depression (α = .70–.74; test–retest reliability = .51–.53) and anxiety scales (α = .70–.83; test–retest reliability = .65–.77). As with the DISC-YC, scales used included those for ADHD symptoms (combined, inattentive and hyperactive/impulsive), ODD, anxiety and depression.

**DuPaul ADHD Rating Scale**

The ADHD Rating Scale (DuPaul et al., 1998) provided a third measure of ADHD symptoms. This measure has well-developed norms, an α of .92 overall, with test–retest reliability of .85, and shows high levels of criterion and discriminatory validity.

**Eyberg Child Behavior Inventory**

The Eyberg Child Behavior Inventory (ECBI) (Eyberg & Pincus, 1999) is designed to assess parental report of ODD symptoms. Criterion validity for the ECBI has been assessed and found to be acceptable (test–retest reliability ranges .86–.88; inter-rater reliability, .79–.86; and internal consistency for the subscales ranges from .88 to .95 (Eyberg & Pincus, 1999).

**Procedure**

Recruitment occurred in pediatric practices and schools with preschool programs, during the first wave of data collection when the children were 4 years old. Parents who expressed interest were subsequently contacted by telephone. A home visit was scheduled, and questionnaires were mailed to the family. The home visit included a 45-min observation period followed by the structured parent–child interaction paradigm. A research assistant then conducted the DISC-YC interview, either in English or Spanish, and parents subsequently completed the remainder of the questionnaires. The total duration of the home visit was about 2.5 h. Procedures were approved by the Institutional Review Boards of the authors’ institutions.

**Data Analyses**

For measures of psychopathology, multivariate analyses of variance were conducted with the three measures of emotional or behavior problems entered as dependent variables and smoking during pregnancy, risk factors described above, and the child’s gender entered as predictors. If the overall effects on the measure of psychopathology were significant, then the results for each individual measure of psychopathology were examined. For the analysis of NA, linear regression was used because there was only one measure of NA. The interaction of gender with smoking during pregnancy was also examined. If the prenatal smoking x gender interaction was significant, then gender effects were examined in all subsequent analyses. Given the large number of comparisons, a Bonferroni-type sequential Sidak correction for multiple comparisons (Sidak, 1967) was
used for hypothesis testing, while noting all findings for which the traditional $p$ value of .05 was achieved. With that correction, a value of $p < .00365$ was adopted. SPSS 17.0 was used in data analysis.

**Results**

**Descriptive Statistics for Outcome Measures**

As expected in a community sample, scores on each of the outcome measures varied widely. If the sample included children with high level of behavior or emotional disorders, ~10% of the sample should obtain scores that exceed the cutoff score for the 90th percentile in the standardization sample. Cutoff scores for the 90th percentile are available for the CSI, and the percent above the 90th percentile cutoff approximated 10% for ADHD-I (10.0%, $n = 68$), ADHD-H (10.2%, $n = 69$), ADHD-C (9.5%, $n = 65$), ODD (9.4%, $n = 64$). The rates for internalizing disorders were slightly lower (GAD, 6.2%, $n = 42$; SAD, 6.6%, $n = 6.6%$; MDD, 2.5%, $n = 17$; Dysthymia, 8.8%, $n = 60$), but the full range of scores were obtained on the internalizing disorders scales. The mean, standard deviation, and range for each CSI scales were: ADHD-I, $M = 5.87$, $SD = 4.18$, $R = 0–25$; ADHD-H, $M = 7.32$, $SD = 5.1$, $R = 0–27$; ADHD-C, $M = 13.2$, $SD = 8.42$, $R = 0–27$; ODD, $M = 5.13$, $SD = 3.63$, $R = 0–24$; GAD, $M = 4.86$, $SD = 3.37$, $R = 0–28$; SAD, $M = 2.21$, $SD = 2.68$, $R = 0–20$; MDD, $M = 1.14$, $SD = 1.62$, $R = 0–13$; Dysthymia, $M = .76$, $SD = 1.23$, $R = 0–9$.

**Relationship Between Smoking During Pregnancy and Behavior Problems Without Controls**

**Externalizing Disorders**

When covariates were not included (Table I), the effects of smoking during pregnancy were significant overall for ADHD-I at the traditional $p < .05$ level, but not after correcting for multiple comparisons. Smoking effects were not significant for ADHD-H or ADHD-C. The results for each of the individual measures of ADHD-I were also significant for smoking during pregnancy. In the multivariate analyses, gender effects were significant for each type of ADHD, with boys showing more ADHD symptoms than girls for all three types. The prenatal smoking x gender interaction, however, was not significant for any type of ADHD symptoms.

The relationship between smoking during pregnancy and symptoms of ODD were not significant, nor were there significant gender or prenatal smoking x gender interactions for ODD.

<table>
<thead>
<tr>
<th>Type of emotional/behavioral problem</th>
<th>Prenatal smoking F-value</th>
<th>Gender F-value</th>
<th>Prenatal smoking x gender F-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD-combined symptoms</td>
<td>4.59***</td>
<td>1.31</td>
<td></td>
</tr>
<tr>
<td>Multivariate test results</td>
<td>4.82*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISC-YC symptoms</td>
<td>7.66**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms</td>
<td>12.60****</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD-hyperactive/impulsive symptoms</td>
<td>2.90*</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Multivariate test results</td>
<td>3.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISC-YC symptoms</td>
<td>5.39*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms</td>
<td>8.32***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Du Paul symptoms</td>
<td>12.03****</td>
<td>14.00****</td>
<td></td>
</tr>
<tr>
<td>Oppositional defiant symptoms</td>
<td>0.58</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Multivariate test results</td>
<td>1.41</td>
<td>1.31</td>
<td></td>
</tr>
<tr>
<td>Anxiety symptoms</td>
<td>2.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISC-YC symptoms</td>
<td>10.21****</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms (generalized anxiety)</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms (separation anxiety)</td>
<td>1.78</td>
<td>4.59***</td>
<td></td>
</tr>
<tr>
<td>Depression symptoms</td>
<td>3.78**</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>Multivariate test results</td>
<td>7.75**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISC-YC symptoms</td>
<td>3.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms (depression)</td>
<td>5.13*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSI symptoms (dysthymia)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note.** *p < .05; **p < .01; ***p < .005; ****p < .001.

**Internalizing Disorders**

The relationships between smoking during pregnancy and symptoms of both anxiety and depression were not significant in the multivariate analyses. Gender effects were significant and higher for boys, but prenatal smoking x gender interaction effects were not significant.

**Negative Affect**

The effect of smoking during pregnancy on NA approached significance ($\beta = .098$, $t = 2.55$, $p = .011$) when corrected for multiple comparisons, while the gender ($\beta = .04$, $t = 1.04$, $p = .30$) and prenatal smoking x gender interactions ($\beta = -.112$, $t = .91$, $p = .36$) were not significant.

**Correlates of Smoking During Pregnancy**

The relationship between smoking during pregnancy and demographic and psychosocial variables related to a variety of child psychiatric disorders were then examined. Among demographic correlates, smoking during pregnancy was
related to lower levels of SES, \( t(677) = 4.47, p = .001 \). There were also race differences, \( X^2(2) = 15.02, p = .001 \), with a higher percentage of smoking among African American mothers (\( n = 18, 15.9\% \)) than among non-Hispanic Whites (\( n = 22, 5.2\% \)), or Hispanic white mothers (\( n = 10, 6.9\% \)). Birth weight, \( t(677) = .98, p = .33 \), was not related to smoking during pregnancy.

Among family climate variables, family stress, \( t(677) = 3.19, p = .002 \) and maternal depression, \( t(677) = 2.86, p = .006 \) were associated with smoking during pregnancy. There was no relationship, however, between family conflict and smoking during pregnancy, \( t(677) = .40, p = .69 \). Smoking during pregnancy was not associated with parental support/engagement, \( t(677) = .02, p = .98 \). Hostility and smoking during pregnancy were significantly related, \( t(677) = 2.38, p = .035 \) at the traditional \( p \)-value level but not when corrected for multiple comparisons. Smoking during pregnancy was not associated with support/scaffolding skills, \( t(677) = 1.94, p = .053 \). There was a significant relationship between smoking during pregnancy and less secure attachment, \( t(677) = 3.41, p = .001 \).

### Models of Prenatal Smoking Effects on Emotional/Behavioral Problems, Including other Demographic and Psychosocial Variables

Prior to examining models that included other demographic and psychosocial variables with smoking during pregnancy, we examined the correlations between psychosocial risk factors (Table II). All but one of the correlations was low to moderate even when significant, suggesting that the risk factors were largely independent of one another. The correlation between life stress and maternal depression however was moderate in size (\( r = .62 \)). In addition, \( t \)-test results described above indicated that both life stress and maternal depression were significantly associated with smoking during pregnancy. The moderately strong relationships between these variables raised the possibility that suppression effects could occur in regression analyses if both stress and maternal depression were entered simultaneously along with prenatal smoking. Suppression occurs when the relationship of one predictor variable to the criterion variable is altered when it is corrected for its correlation with another variable. When suppression is present, the magnitude of the relationship between the predictor and criterion variable may be reduced or can even reverse the direction of the relationship. Suppression can be examined by removing one of the predictor variables from the regression equation (Kline, 1998). We tested for this possibility in models where the effects of smoking during pregnancy were significant. We examined the effects of smoking during pregnancy in regression models that included demographic (SES, race dummy coded), family climate (family conflict, stress), maternal depression, parenting (maternal support/engagement, maternal hostility, maternal support/scaffolding skills, child attachment), and child birth weight. Models were tested only for ADHD-I, for which smoking during pregnancy showed a significant relationship when covariates were not included, and for NA, because the effects of smoking during pregnancy on NA approached the significance level for multiple comparisons, we elected to conduct the analysis of NA when psychosocial covariates were added.

### ADHD-I

As Table III indicates, the effect of smoking during pregnancy on ADHD-I was significant \( (p = .048) \) at the traditional \( p \)-value level, when demographic, family climate, maternal depression, parent–child interaction, and child factors were included in the model, but was not significant at the \( p = .01 \) level for multiple comparisons. To examine the possibility that suppression effects were present, the analysis was repeated with life stress eliminated and
the effects of smoking during pregnancy still were not significant.

Other psychosocial variables were significantly associated with ADHD-I symptoms, including race (African Americans higher than non-Hispanic whites), lower SES, higher family conflict, maternal depression, higher maternal hostility, lower support/engagement, poorer maternal support-scaffolding, and less secure attachment.

Negative Affect
Smoking during pregnancy was not significantly associated with NA when the psychosocial covariates were included, among those psychosocial risk factors, race (being Hispanic rather than non-Hispanic white), family conflict, less maternal support/engagement, and more maternal hostility were significantly associated with NA.

Discussion
The present study examined the relationship between smoking during pregnancy and behavior and emotional problems in a community sample of 4-year-old children. This study differed from most prior research in the use of a large, diverse sample, the age of the children participating in the study, the range of psychosocial factors studied, and the use of multiple measures of child psychopathology. The findings having implications for our understanding of the relationship between smoking during pregnancy and child psychopathology, as well as implications for the design of future studies in this area.

First, in the present study, the relationship between smoking during pregnancy and symptoms of ODD in preschoolers was not significant, even without including other risk factors and correlates of smoking during pregnancy. While a small number of other studies of preschool children have reported a significant relationship between smoking during pregnancy and externalizing problems, all (Day et al., 2000; Huijbregts et al., 2007; O’Callaghan et al., 1997; Orlebeke et al., 1997; Wakschlag & Keenan, 2001) but one (Wakschlag et al., 2006) failed to control for at least one covariate in each area of demographic, parental psychopathology, parenting, family stress, and pre-/perinatal factors, and the latter study was limited by a lack of racial/ethnic diversity in the sample. Thus, overall, there is little evidence for a main effect of smoking during pregnancy on oppositional behavior in preschool children.

Second, the present study failed to find a significant relationship between smoking during pregnancy and either ADHD-H or ADHD-C, and the relationship between smoking during pregnancy and ADHD-I was not significant after including a wide range of covariates. While these results differ from prior studies (Huijbregts et al., 2007; McGee & Stanton, 1994; Romano et al., 2008; Streissguth et al., 1984), those studies failed to include the range of variables included in the present study.

Third, consistent with three prior studies, the present study failed to find a relationship between smoking during pregnancy and internalizing disorders. Collectively, these studies provide little evidence for an association of smoking during pregnancy with these types of disorder.

Fourth, the present study does not support the developmental model proposed by Nigg and Breslau (2007). That model posited that smoking during pregnancy contributes to temperamentally-based NA in young children which, combined with problems in parent–child relationships, mediates the relationship between smoking during pregnancy and the later development of ODD symptoms. If NA serves as a mediator, then the relationship between the independent variable (smoking during pregnancy) and the mediator (NA) should be statistically significant (Baron & Kenny, 1986). The results of the present study do not support this model because there was a nonsignificant effect for smoking during pregnancy on NA in young children when controlling for theoretically and empirically related covariates.

However, while the results of the present study do not support a relationship between smoking during pregnancy and behavior problems in preschool children, it is possible that direct effects of smoking during pregnancy on behavior and emotional problems do not emerge until children are school age or older. While ODD in preschoolers.

| Table III. Multivariate Analyses of Prenatal Smoking Effects |
|-----------------|-----------------|-----------------|
| F-value | ADHD-I F-value | ADHD-I* F-value | Negative affect t-value |
| Prenatal smoking | 2.65* | 2.55 | 1.40 |
| Race (Dummy 1) African American versus non-Hispanic White | 14.41*** | 15.32*** | 1.81 |
| Race (Dummy 2) Hispanic versus non-Hispanic White | 1.76 | 1.84 | 2.27* |
| SES | 2.98* | 2.81* | 6.8 |
| Life stress | 2.52 | – | 1.27 |
| Family conflict | 6.08*** | 7.02*** | 2.08* |
| Maternal depression | 6.83*** | 11.92*** | 1.97* |
| Maternal support-engagement | 4.92** | 4.92** | 3.14** |
| Maternal hostility | 10.23*** | 10.22*** | 2.10* |
| Maternal support-scaffolding skills | 3.13* | 3.06* | 1.76 |
| Attachment security | 10.83* | 11.10*** | 20 |
| Birth weight (grams) | .34 | .33 | .49 |

Note. *Life stress variable removed to test for suppression effects. *p < .05; **p < .01; ***p < .001.
is reasonably stable, ODD symptoms do decline in some children at about age 5 years (Lavigne et al., 1998), and the direct effects of smoking during pregnancy on ODD and other externalizing problems and ADHD might only become apparent among those children with ODD persisting into, or beginning in, the school years.

Finally, the present study demonstrates the importance of including a wide range of variables that are associated with the development of child psychopathology in order to estimate the effects of smoking during pregnancy. While prior studies typically included demographic and child health variables, and often assessed maternal psychopathology and some aspects of family climate, important aspects of mother–child interaction patterns, particularly those required to promote secure attachment, have been ignored. When the full range of variables was included in the present study, reducing the effects of omitted variables, the effects of smoking during pregnancy for ADHD-I that had appeared significant no longer were. This is not entirely surprising. Wakschlag et al. (2002) had raised concerns about confounding variables in studying the effects of prenatal smoke exposure, concerns about the effects of omitted variables in study psychopathology have been noted before (Tomarken & Waller, 2003), and the results of the present study are consistent with those predicted by D’Onofrio et al. (2008), who argued that the relationship between smoking during pregnancy and measures of child psychopathology would be associated with environmental risk factors other than those which had been studied previously. The results of the present study suggest a wide range of correlates of prenatal smoke exposure, including child attachment, should be included when studying the effects of smoking during pregnancy.

The two main limitations of the present study involve the use of retrospective reports of smoking and the inability to assess dose effects of exposure to smoking during pregnancy. The present study used the retrospective report of smoking during pregnancy from the Smoke-Free Families clinical trial (Melvin et al., 2000) and classified the children as exposed versus non-exposed. We followed this procedure because our confidence was greater that mothers would more accurately recall whether or not they had smoked during pregnancy than the number of cigarettes they typically smoked at that time, and studies have indicated that maternal recall for smoking during pregnancy is good even over long periods of time. In addition, if the measure used in the present study was not at all valid, then significant correlations between many of the known psychosocial correlates of smoking and prenatal smoke exposure obtained with the measure used in the present study would not have been significant. However, contemporaneous reports of smoking during pregnancy are still to be preferred to retrospective reports. The “caveat” to be taken from this report is that a wide range of psychosocial correlates needs to be included in future studies on the effects of smoking during pregnancy when contemporaneous or retrospective measures of smoking are used.

A second major limitation concerns the possibility of dose effects. Most studies of compared exposed to unexposed children, other studies have identified a dose effect, with behavior problems emerging if mothers were relatively heavier smokers. Since the present study did not examine dose effects, it is possible that there is a dose effect for smoking during pregnancy not detected in the present study. The most important finding of the present study is that, since the inclusion of the wide range of psychosocial variables, particularly parenting variables and attachment, examined in the present study showed no effect of prenatal smoke exposure versus non-exposure, future studies of dose effects for prenatal smoke exposure need to examine these same critical variables to be definitive. Thus far, studies (Ashford et al., 2008; Button, Thapar, & McGuffin, 2005; D’Onofrio et al., 2008; Day et al., 2000; Fergusson, Horwood, & Lynskey, 1993; Fergusson, Woodward, & Horwood, 1998; Maughan, Taylor, Caspi, & Moffitt, 2004; Silberg et al., 2003; Streissguth et al., 1984; Thapar, Fowler, Rice, & al., 2003; Wakschlag et al., 2006; Weitzman et al., 1992; Williams et al., 1998) showing a dose-effect relationship with stronger effects for heavier prenatal smoke exposure have failed to do this, so the problem of “omitted variables” in dose-effect studies remains. Future studies of dose-effect relationships need to include a sufficiently broad representation of psychosocial factors associated either with smoking or the development of behavior problems to assess the strength of the relationship between smoking during pregnancy and child psychopathology.

A third limitation involves the use of a single parent informant for many of the risk factors. The use of a single informant increases the possibility that significant results are inflated due to common method variance. However, this was certainly not the case in the present study because the main findings involved an absence of significant relationships between the variables, so it is unlikely that inflated effects sizes due to common method variance significantly impacted the results. Also, in addition to maternal-report, we used direct observation to examine several of the risk variables included in this study (i.e., parent scaffolding, child attachment).

The strengths of this study include attention to preschoolers, the wide range of covariates studied, the
assessment of both externalizing and internalizing disorders in young children, the use of multiple measures of outcome rather than reliance upon a single measure, and the inclusion of a large, diverse community sample. These results highlight the importance of carefully selecting theoretically relevant, empirically tested variables that may serve as mediators in the relationship between smoking during pregnancy and child internalizing and externalizing problems. This is consistent with current approaches in developmental psychopathology, in which researchers are turning their attention to the interaction between biological and psychosocial variables as causal factors in child disorders, rather than focusing on only one of these aspects of human functioning (Cicchetti & Curtis, 2007).

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of genetic and environmental confounds. Development and Psychopathology, 20, 139–164.


