Maternal Smoking during Pregnancy and Risk to Boys’ Conduct Disturbance: An Examination of the Causal Hypothesis

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Background: We undertook this study to determine whether the widely replicated link between maternal smoking and conduct disturbance (Cd) is better explained by a model of direct causation or of mother–offspring transmission of a latent Cd variable.

Methods: Family data collected on 538 adolescent twin boys from the Virginia Twin Study of Adolescent Behavioral Development (VTSABD) was used to compare two alternative models: 1) a model composed of a latent transmissible factor that influences mother’s juvenile conduct symptoms, smoking during pregnancy, and subsequent Cd and smoking in her adolescent boys; and 2) a model specifying a direct causal path from mother’s smoking to child Cd.

Results: The maternal–offspring transmission model fit the data as well as a model specifying a direct causal path from maternal smoking to child Cd.

Conclusions: Our results suggest that the association between maternal smoking during pregnancy and boys’ Cd symptoms may be attributed to the transmission of a latent Cd factor and not to a direct effect of the smoking. Our results challenge previous findings of a direct effect of prenatal smoke exposure on risk to Cd once other etiologic factors are considered. Biol Psychiatry 2003;53: 130–135 © 2003 Society of Biological Psychiatry

Key Words: Maternal smoking, boys Cd, familial transmission

Introduction

Numerous aspects of the prenatal environment including low birth weight, prematurity, obstetric complications, physical anomalies, maternal illness, nutritional status, and substance and medication use have been associated with behavioral disturbances in childhood and adolescence (Rutter et al 1998). More recently, maternal smoking during pregnancy has been implicated as an important risk factor for children’s behavioral problems (Brennan et al 1999; Fergusson et al 1993, 1998; Wakschlag et al 1997; Weissman et al 1999; Weitzman et al 1992). Despite cogent evidence for an association across a wide range of samples, developmental stages, and outcomes, the establishment of a direct causal link between prenatal smoke exposure and conduct disturbance (Cd) has not yet been unequivocally demonstrated. Possibly, the association between smoking in pregnancy and child Cd may be explained by a third transmissible factor, such as antisocial behavior, that influences both mother’s smoking during pregnancy and subsequent conduct problems in her children. Although such variables as parental criminal history (Brennan et al 1999; Fergusson et al 1993, 1998), antisocial personality (Wakschlag et al 1997; Weissman et al 1999), and psychiatric hospitalization (Brennan et al 1999) have all been included as potential confounds, they may have been limited in their assessment of maternal antisocial behavior. If the measure of maternal antisociality does not adequately index transmissible factors that influence both smoking during pregnancy and subsequent child conduct problems, or if there are different etiologic factors influencing antisocial behavior in childhood and adulthood (Lyons et al 1995), it would not serve as an adequate control.

Our analysis was undertaken to address further whether prenatal smoke exposure has a direct impact on childhood conduct disturbance. Using family data collected on 538 adolescent boys from the Virginia Twin Study of Adolescent Behavioral Development (VTSABD), we sought to...
determine whether the widely replicated association between maternal smoking during pregnancy and child Cd is better explained by a model involving direct environmental causation or, alternatively, parent–offspring transmission of a latent variable (i.e., antisocial behavior). Toward this goal, mother’s retrospective report of her own childhood symptoms of conduct disorder was included as an index of a putative latent variable that contributes to smoking during her pregnancy and conduct problems and smoking in her adolescent son. Because different etiologic factors are likely influencing antisocial behavior in childhood and adulthood (Lyons et al. 1995), we included a measure of maternal antisocial behavior that would be comparable to antisocial behavior assessed in the child.

Methods and Materials
The Virginia Twin Study of Adolescent Behavioral Development (VTSABD) is a multiwave, longitudinal follow-up study of psychopathology in a population sample of juvenile twins and their parents. The study was originally designed to understand the role of genetic and social factors in the development of psychiatric problems in children and adolescents. Beginning in 1987, with the assistance of the Commonwealth Department of Education, we were supplied with the names and addresses of all putative twin pairs enrolled in state schools. After eliminating pairs who turned out not to be twins, had left the state, were outside the age window (8–16), or who were not Caucasian, an eligible population of 1894 twin pairs was identified who comprised the target population for a Wave 1 interview. Between January 1990 and December 1993, we were able to conduct home interviews with 1413 (79%) of these families. Further details concerning the method of ascertainment, sample structure, assessment protocol, and participation rates have been presented elsewhere (Eaves et al. 1997; Hewitt et al. 1997; Meyer et al. 1996; Simonoff et al. 1997). The study was approved by Virginia Commonwealth University’s Committee for the Conduct of Human Research (CCHR #8802-3G). During the visit, the study goals were reviewed, the interview process explained, and informed consent obtained from parents; assent was obtained from children aged 14 years or older. Although genetically informative data were collected, genetic models of parent–offspring resemblance were not attempted because fathers’ report of their own smoking was not assessed as part of the home interview. Only the familial relationship between mothers smoking and their sons’ behavior was analyzed using data collected from the first wave of the study.

Measures
During the initial home interview, mothers were asked a series of pregnancy-related questions including length of gestation, twins’ birth weight, and whether she smoked during the pregnancy. If smoking was reported, the mother was asked whether she smoked more than 10 cigarettes per day for at least 1 month. A trichotomous scale was developed comprised of those women who did not smoke (0), those who smoked less than 10 cigarettes a day for 1 month or more of the pregnancy (1), and those who smoked more than half a pack of cigarettes per day for at least 1 month of the pregnancy (2).

Conduct disturbance was based on the child’s report of symptoms of DSM-III-R–based conduct disorder from the Child and Adolescent Psychiatric Assessment (CAPA; Angold et al. 1995). The individual conduct symptoms were coded as either present (1) or absent (0) in the previous 3 months, depending on their expression in at least two of the child’s activities and their degree of uncontrollability. The 10 symptoms were then summed to form a quasicontinuous Cd scale.

Mother’s retrospective report of their own conduct disorder symptoms as teenagers was collected as part of a structured interview designed to assess antisocial personality disorder. The symptoms comprising a DSM-III-R diagnosis of conduct disorder were summed into a semicontinuous measure of Cd, comparable to the questions used to assess Cd in the child interview.

A measure of the child’s smoking behavior was also included as an additional index of the putative latent variable of antisociality that influences maternal smoking in pregnancy and is transmitted from mothers to their adolescent sons. It was based on the ratings from mothers, fathers, and the child using the CAPA interview. If any of the three informants reported that the child smoked at least one whole cigarette in the previous 3 months, he was considered to have smoked.

Statistical Methods
The associations among childhood Cd symptoms; maternal smoking during pregnancy; retrospectively reported symptoms of maternal Cd; twins’ age, birth weight, gestational age; and child smoking were estimated using the software package PRELIS (Jöreskog and Sörbom 1996). The polychoric correlations between pairs of categoric measures (e.g., maternal smoking and child smoking), the polyserial correlations between continuous and categorical variables (e.g., birthweight and child Cd), and the Pearson correlations between two continuous measures (birthweight and gestational age) were computed. For the noncontinous variables, these correlations assume a hypothesized underlying bivariate normal distribution of liability categorized by the imposition of one or more arbitrary thresholds in each dimension. For subsequent model fitting, only those variables that were significantly correlated with childhood conduct symptoms were retained.

For assessing the relative contributions of putative risk factors on children’s Cd and to correct for the nonindependence of data from twins of a pair, the SAS PROC MIXED procedure was used (SAS 6.12; SAS Institute 1996). This procedure was employed to take account of the cross-twin covariances as part of the fitted model and to estimate the Type III SS or partial sums of squares (SS) for evaluating the independent effect of an individual variable over and above that contributed by the other variables in the model.

A series of latent variable structural equation models were then next fitted to the data using the statistical program Mx (Neale et al. 1999). As shown in Figure 1, the full latent variable model specifies a latent variable or factor that is transmitted.
across generations (path b) from the mother (Mother) to her twin boys (Twin 1/Twin 2). This latent variable is correlated with the mother’s history of juvenile Cd (h) and influences smoking during her pregnancy (path a) and Cd (c) and smoking (e) through a latent twin factor. The model also includes the direct path (d) from maternal smoking in pregnancy to boys’ Cd. A residual correlation between this latent twin factor (f) twin 1’s and twin 2’s smoking (g) is also included. Eliminating path d represents a test of the primary hypothesis, that is, whether maternal smoking in pregnancy has a direct effect on child Cd over and above that explained by the latent maternal factor reflecting adolescent Cd and maternal smoking that is transmitted from mothers to their adolescent sons.

Figure 1. Full latent variable transmission model. The full latent variable transmission model comprises a latent maternal risk factor (Mother) reflecting maternal adolescent conduct disturbance (Cd; path h), which influences smoking in pregnancy (path a) and boys Cd (c) and smoking (e) through a latent twin factor. The model also includes the direct path (d) from maternal smoking in pregnancy to boys’ Cd. A residual correlation between this latent twin factor (f) twin 1’s and twin 2’s smoking (g) is also included. Eliminating path d represents a test of the primary hypothesis, that is, whether maternal smoking in pregnancy has a direct effect on child Cd over and above that explained by the latent maternal factor reflecting adolescent Cd and maternal smoking that is transmitted from mothers to their adolescent sons.

The models were fit to the transformed raw data by the method of maximum likelihood pedigree analysis (Lange et al 1976). When model fitting to categorical data, Mx can provide the maximum likelihood (ML) estimates of the thresholds and the parameters of the linear model for the hypothesized relationships between the latent liability dimensions.

**Results**

The ages of the twin boys ranged from 12 through 17 with a mean of 14.02. The average number of weeks of gestation was 37.83, which is reasonably consistent with previous studies showing that twins tend to be about 3 or 4 weeks premature and weigh about 30% less than singletons (Plomin et al 1990).

Of the mothers, 26% said that they smoked during their pregnancy (n = 140), and the majority of these, 83% (n = 117), reported that they smoked more than a half a pack of cigarettes per day for at least 1 month, rates generally comparable to those reported in other studies (Brennan et al 1999; Wakschlag et al 1997). Figure 2 shows the mean rate of child Cd symptoms among the children of mothers who did not smoke, those who smoked less than 10 cigarettes daily, and those who smoked at least half a pack of cigarettes for a minimum of 1 month during the pregnancy. The rate of Cd in the children of mothers who reported that they did not smoke was .55, nearly identical to the rate of Cd in the boys of mothers who smoked less than 10 cigarettes daily (.56). In contrast, the average number of conduct-disordered symptoms in boys of mothers who reported smoking at least half a pack of cigarettes for a minimum of 1 month was .80, significantly higher than the other two groups, p < .05. Maternal Cd symptoms correlated -.02 with smoking less than half a pack of Cd (path d) was compared with a reduced model without this parameter. The difference between $-2\log$(log-likelihood) of the two models is distributed as a chi-square ($\chi^2$), with degrees of freedom ($df$) equal to the difference in the number of parameters estimated in the two models.

Figure 2. Maternal smoking in pregnancy and average number of boys’ conduct disturbance (Cd) symptoms (N = 538).
cigarettes, but correlated .18 with smoking 10 or more cigarettes for at least 1 month of the pregnancy, comparable to odds ratios of .83 (p < H11005 .56) and 2.4 (p < H11021 .0001), respectively.

**Phenotypic Correlations**

Because only smoking more than 10 cigarettes per day was significantly related to child Cd, those women who smoked less than 10 cigarettes were combined with the nonsmokers for the remaining analyses. The phenotypic correlations shown in Table 1 indicate significant and positive associations between smoking more than 10 cigarettes during pregnancy for at least 1 month and 1) mother’s juvenile Cd symptoms, 2) low birth weight and gestational age, and 3) boy’s Cd. Child’s Cd is as much related to mother’s Cd as it is to mother’s smoking during her pregnancy. Although maternal smoking is correlated with perinatal risk, low birth weight and prematurity are not associated with subsequent Cd symptoms. Boy’s smoking is significantly correlated with conduct-disordered behavior and mother’s smoking, but not with mother’s history of Cd.

**General Linear Model**

Table 2 presents the results from fitting a series of general linear models to the data using SAS PROC MIXED. Only age, maternal smoking in pregnancy, maternal Cd, and child smoking were included in the models, given their significant association with boy’s Cd. Three models were analyzed. The first revealed a statistically significant effect of smoking during pregnancy on boy’s Cd when controlling for age. In model II, when mother’s childhood conduct problems were added, the effect of smoking was no longer statistically significant. In model III, when the child smoking variable was included, the effect of maternal smoking was further attenuated. These results suggest that the observed association between maternal smoking and juvenile Cd may be explained by other factors rather than by the impact of smoking itself.

**Latent Variable Model**

In fitting the full latent variable model to MZ and DZ twins separately, all but the residual correlation between the twins’ latent variable could be constrained to be equal across the two groups, $\chi^2_{\text{diff (17)}} = 13.05, p > .05$ (rMZ = .65; rDZ = .31). To test the primary hypothesis of this analysis, eliminating the direct path from maternal smoking to child Cd (path d) did not result in a significant worsening of fit of the model, $\chi^2_{\text{diff (1)}} = 1.24, p > .05$. The standardized estimates under this best fitting reduced model are shown in Figure 3. This model reveals a strong association between the latent mother antisocial risk vari-

Table 1. Correlations between Boy’s Conduct Disturbance (Cd), Birth Weight, Gestational Age, Maternal Juvenile Cd, Maternal Smoking in Pregnancy, and Child Smoking (N = 538)

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Child Cd</th>
<th>Birth Weight</th>
<th>Gestational age</th>
<th>Maternal Cd</th>
<th>Maternal Smoking</th>
<th>Child Smoking</th>
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<tr>
<td>Birth Weight</td>
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<td></td>
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<tr>
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<td>.62c</td>
<td>1.0</td>
<td>.03</td>
<td>1.0</td>
<td></td>
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<tr>
<td>Maternal Juvenile Cd</td>
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<td>.16b</td>
<td>-.02</td>
<td>-.19c</td>
<td>.27c</td>
<td>1.0</td>
<td></td>
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<tr>
<td>Maternal Smoking</td>
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<td>.19b</td>
<td>-.29c</td>
<td>-.19c</td>
<td>.27c</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
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<td>.61c</td>
<td>-.03</td>
<td>.07</td>
<td>.01</td>
<td>.22b</td>
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</tr>
</tbody>
</table>

aTen or more cigarettes/day for at least 1 month of pregnancy.

b p < .01.

c p < .001.

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Table 2. Results from Regressing Boys’ Conduct Disturbance (Cd) Symptoms on Maternal Smoking in Pregnancy, Maternal Juvenile Cd Symptoms, and Child Smoking

<table>
<thead>
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<th>Source</th>
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<th>Pr &gt; F</th>
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</thead>
<tbody>
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<td>Model II</td>
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<td>Maternal Smoking</td>
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<tr>
<td>Maternal Cd</td>
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<td>.03</td>
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<tr>
<td>Model III</td>
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<td>Age</td>
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<td>Maternal Smoking</td>
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<tr>
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<tr>
<td>Child Smoking</td>
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Within each model, the (Type III) sums of squares (SS) represent the partial contribution of each effect in the model, controlling for every other effect. Significance of each item in the model is assessed by an F test of the Type III mean squares against the residual mean square. The probabilities tabulated (Pr > F) are the significance levels of the F ratios derived from the corresponding Type III sums of squares.
able and smoking during pregnancy (.86) and a moderate association with maternal Cd (.35). This latent transmissible variable also significantly influences juvenile Cd and smoking in the adolescent twins (.41); dropping this path results in a significant worsening in the fit of the model, \( \chi^2_{\text{diff}} (1) = 18.94, p < .001 \). These findings suggest that the demonstrable link between maternal smoking and child Cd can be explained by the intergenerational transmission of a latent antisocial factor rather than to a direct effect of smoking in pregnancy.

**Discussion**

The results from this study are consistent with a growing literature in reporting a significant association between maternal smoking during pregnancy and boys’ Cd. In contrast to previous studies, however, we find that the effect of prenatal smoke exposure on juvenile Cd is not significant when other familial factors are considered. (This pattern of results has also been replicated using maternal ratings of externalizing behavior from the Child Behavior Checklist (Achenbach and Edelbroch 1979) collected on a portion of the VTSABD sample before the first home interview.) This is not to imply that smoking during pregnancy does not have deleterious effects on the fetus; rather, our data suggest that it may not have a direct effect on conduct problems in adolescence. The development of Cd in childhood appears to be related to the familial transmission of some other risk variable(s) other than smoking in pregnancy.

A dose-response relationship was found between maternal cigarettes smoking and boys’ Cd; Cd was associated with smoking more than a half a pack of cigarettes but not associated with smoking fewer than 10 cigarettes. Maternal Cd symptoms were also significantly correlated only with these higher levels of smoking, consistent with maternal smoking during pregnancy representing a symptom of the familial transmission of conduct disorder and not necessarily a direct risk factor itself.

The discrepancy between these findings and the results of other studies may be due to a number of methodologic differences. In our study, a latent variable analytic approach was used. Moreover, the latent factor influencing maternal Cd and smoking during pregnancy may represent a better index of transmissible factors that influences risk to Cd in the children. We also conducted a separate analysis that included a measure of adult antisocial personality comparable to that used in previous studies. Consistent with past research, this variable did not attenuate the association between smoking in pregnancy and Cd in the boys as did maternal juvenile conduct disorder. Thus, because our measure of maternal antisociality may be more etiologically comparable with antisocial behavior assessed in the adolescent boys, it may have served as a more powerful control. The inclusion of boys’ smoking as another manifestation of the underlying latent variable reflecting both smoking in pregnancy and maternal Cd was also a significant addition to the model.

An important limitation of this study is its reliance on a retrospective report of smoking during pregnancy. Besides the obvious potential inaccuracies in remembering pregnancy-related events 12 years or more in the past, it may be the same tendencies toward antisocial behavior that also influence an individual not to report smoking while pregnant.

This analysis also did not use the genetic relationship between mothers and their twin boys in elucidating the nature of the latent variable linking smoking and Cd. The conventional twin–parent design has important methodologic limitations in identifying the causes of parent–offspring resemblance. Ideally, it will require other kinship designs (e.g., the children of twins; Eaves et al 1999; Heath et al 1985) to determine whether the transmission of risk from mothers’ to their sons’ Cd is genetically or environmentally mediated. Our findings clearly warrant further investigation of the underlying causes of transmissible risk linking maternal smoking and child Cd using these other designs.

Although this study shows that smoking during pregnancy does not have a direct effect on the development of behavioral problems in adolescence, it does not mitigate the many studies linking smoking during pregnancy to a multitude of other poor outcomes. Even if additional studies support these findings, smoking during pregnancy would remain inadvisable given the evidence for increased
fetal and infant mortality (Chatenoud et al 1998; Cooke 1998; DiFranza and Lew 1995), low birth weight (Pollock et al 2000; Secker-Walker et al 1998), and intellectual deficits throughout development (Fogelman and Manor 1988; Rantakallio 1983); however, we should note that these studies do not provide incontrovertible evidence for the deleterious effects of these variables, given the lack of adequate control of possible confounding factors.

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