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Prenatal Exposure to Maternal and Paternal Smoking on Attention Deficit Hyperactivity Disorders Symptoms and Diagnosis in Offspring

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Abstract

The study examined the effect of maternal and paternal smoking during pregnancy on the child's inattention and hyperactivity/impulsivity symptoms, and the risk for attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). Generalized estimating equations, incorporating data from multiple informants (parents and teachers), was used to evaluate levels of ADHD as a function of parental smoking. The risk for ADHD, ODD, and comorbid ADHD and ODD was evaluated using polytomous logistic regression. We found that maternal, but not paternal, smoking was significantly associated with elevated inattention, hyperactivity/impulsivity, and total ADHD symptoms in children. Children of smoking, relative to nonsmoking, mothers had a significant increased risk for comorbid ADHD and ODD and ADHD, but not ODD. Although father's smoking was not associated with an increased risk, as it strongly influenced mothers' smoking, intervention for both parents may be most effective in preventing the pathway to ADHD-related problems in the children.

Keywords

Smoking during pregnancy; inattention; hyperactivity/impulsivity; ADHD; ODD

Attention deficit hyperactivity disorder (ADHD), characterized by inattentiveness and/or hyperactivity/impulsiveness, has an estimated prevalence of 3% to 10% among school-age children (Pastor and Reuben, 2008; Rowland et al., 2002; Scahill and Schwab-Stone, 2000). Further, it is widely recognized that the behavior characteristic of ADHD usually emerge during the preschool years (Barkley, 1990; Campbell, 1995; Lahey et al., 1994), and the condition is highly heritable and familial (Faraone et al., 2005; Goodman and Stevenson, 1989; Rhee et al., 1999).

Despite high heritability, clinical manifestations of childhood ADHD are also associated with numerous environmental factors that may increase risk for ADHD beyond genetic risk. Among these risk factors is prenatal exposure to smoking (Nigg and Breslau, 2007; Newman et al., 1997; Schmitz et al., 2006; Vuijk et al., 2006; Romano et al., 2006; Huizink and Mulder, 2006; Linnet et al., 2005; Button et al., 2005). Although maternal smoking, particularly during pregnancy, is considered to be the single largest modifiable lifestyle risk

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factor for adverse child development (Baler et al., 2008), pregnancy has not been found to be an effective deterrent to smoking (Haug et al., 1994). Several studies have shown that approximately 10% to 20% of pregnant women, especially those with psychiatric disorders (Goodwin et al., 2007), who have low socioeconomic status (SES) (Phares et al., 2000), are single parents, or have problematic relationships (Goodwin et al., 2007; DiFranza and Lew, 1995; Wakschlag et al., 2003), continue to smoke during pregnancy (DiFranzza and Lew, 1995; Goodwin et al., 2007; Maughan et al., 2004; Wakschlag et al., 2003) despite the well-known risk for perinatal problems such as low birth weight (<2500 g), preterm birth, and intrauterine growth retardation (Newton and Hunt, 1984; Hedegaard et al., 1996; Mutale et al., 1991).

Among the toxic substances cigarettes contain, nicotine is one of the key ingredients known to have adverse effects on fetal growth (Lambers and Clark, 1996). It readily crosses the placenta, with concentrations in the fetus as much as 15% higher than maternal levels (Huizink and Mulder, 2006; Walker et al., 1999), and affects the fetal central nervous system (Stillman et al., 1986). Nicotine cannot only create subtle neurological insults during the formation of the fetal brain (Fergusson et al., 1992), it can also lead to a decrease in the oxygen flow and other nutrients across the placenta by constricting uterine arteries (Lambers and Clark, 1996). Furthermore, prenatal exposure to nicotine results in more nicotine receptors that modulates the development of serotonic and dopaminergic systems in the brain (Marks et al., 1993; Hellstgrom-Lindahl et al., 2001). Nicotinic receptors found in the fetal brain from the first trimester hinder the neural development (Hellstrom-Lindahl et al., 2001; Luck et al., 1985). More specifically, the nicotinic input to the dopaminergic motivational/reward system during critical periods of development predisposes the brain to subsequent deficits resulting in impulse control, attention deficits, and aggression in early childhood or even more than a decade later (Kandel et al., 1994).

Nevertheless, specificity of the association between prenatal exposure to smoking and child behavioral problem outcomes remains unclear. A review of the literature suggests that exposure to maternal smoking in utero is associated with multiple adverse outcomes related to self-regulation (Sanchez et al., 2001; Ladd et al., 2000; Leserman et al., 1996), such as deficits in impulsivity, attention (Linnet et al., 2003; Rodriguez and Bohlin, 2005), and aggression (Wakschlag and Hans, 2002; Wakschlag et al., 2006). Together they may affect behavioral functioning through a cascade of interacting effects. Tarter (2002) hypothesized that the etiological pathways may be caused by neurological injury because of nicotine exposure to the developing fetus's brain, and that in turn causes deficits in cognitive and behavioral competencies. Exposure to nicotine in utero may manifest in a wide range of clinically significant behavioral problems in early childhood and this may not be limited in ADHD. Although considerable empirical evidence indicates the associations between exposure to prenatal smoking and both ADHD and oppositional defiant disorder (ODD), it remains unexplored whether the risk of ODD is increased by smoking because of its high comorbid rates with ADHD, or vice versa. It is also possible that exposure to smoking during pregnancy is directly associated with comorbid ADHD and ODD by directly increasing risks for both.

An examination of the both maternal and paternal smoking status may clarify the etiological basis for ADHD and ODD. For example, if maternal smoking but not paternal smoking is associated with an increased risk for child outcomes, it may tell us that the timing of the exposure (i.e., in utero or fetal period) has an important influence on child behaviors and diagnostic outcomes (ADHD and/or ODD). If exposure to both maternal and paternal smoking is associated with the highest magnitude of risk in diagnostic outcomes, it may suggest that both, more direct in utero exposure and second-hand exposure have adverse effect on optimal neuropsychological development in children. Surprisingly, no study has

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examined the effect of both maternal and paternal smoking during pregnancy on behavioral characteristics associated with ADHD and comorbid ODD. As heritability for ADHD is reported to be high (Faraone et al., 2005), elucidating the relationship with maternal and paternal smoking could provide important insights as to whether exposure to smoking is, in fact, most detrimental in utero. Furthermore, examining comorbid status of ADHD and ODD among children with different types (maternal vs. paternal) cigarette exposure will help clarify whether exposure to nicotine is a risk for specific behavioral disorders such as comorbid ADHD and ODD.

METHOD

Procedures and Participants

The study recruited 214 children as part of a longitudinal study of children at risk for ADHD. The ADHD-Rating Scale-IV (ADHD-RS-IV; DuPaul et al., 1998) was distributed to parents of 3-and 4-year-old children in preschools surrounding Queens College along with consent forms that allowed us to ask the teacher to complete the same scale. Teachers were contacted only after we received parental signed consent. Three children, who were adopted, were excluded; thus all children are biological offspring of participating parents. Two children for whom smoking status of either mother or father during pregnancy was unknown were excluded, resulting in 209 children in the current study.

There were no gender or ethnic restrictions, but children and parents were required to be English-speaking. Children with a Wechsler Preschool and Primary Scale of Intelligence-III Full Scale IQ below 80, a pervasive developmental disorder, a diagnosed neurological disorder, or those who were taking systemic medication for a chronic medical condition (including ADHD) were excluded. The larger project from which this study was derived was approved by the Queens College Institutional Review Board, and parents gave informed consent for their child to participate.

MEASURES

Smoking Status

Developmental history was obtained from parents through a self-report demographic questionnaire. Information about the pregnancy was acquired by a trained interviewer who was blind to the child's clinical ratings; information on both mother's and father's smoking status (yes/no) during the pregnancy was obtained.

ADHD-RS-IV

Parents and teachers completed the ADHD-RS-IV (DuPaul et al., 1998). This checklist consist of the 18 ADHD behaviors in DSM-IV (9 inattention and 9 hyperactive/impulsive items), which were rated on a 4-point scale (0 = not at all; 1 = just a little; 2 = often; and 3 = very often) and captured behavior over the preceding 6 months.

Collapsing across individual items, the mean ADHD-RS-IV School and Home totals were 21.25 (*SD* = 12.97; range = 0–48) and 21.61 (*SD* = 16.62; range = 0–54), respectively. Previous research indicates that this type of checklist is a reliable and valid assessment tool for children with ADHD (Faries et al., 2001) and appropriate for use with diverse populations (Reid et al., 1998). Children's age was unrelated to parent's ($r = 0.11$, $p = 0.21$) and teacher's ($r = 0.06$; $p = 0.47$) report of total ADHD symptoms. Family SES was moderately, but significantly, correlated with parent ($r = -0.24$, $p = 0.002$) and teacher (-0.22, $p = 0.004$) reports of total ADHD symptoms.

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ADHD Diagnosis

The Kiddie-SADS-PL (Kaufman et al., 1996) is a reliable, often used, semi-structured child psychiatric interview that assesses a wide array of psychiatric conditions as outlined in the DSM-IV. The ADHD and ODD modules were administered to the parent by a trained interviewer who was blind to the child's risk status and maternal and paternal smoking status. The Kiddie SADS allows for considerable latitude on the part of the interviewer to query various behaviors and settings: the presence or absence of symptoms is finally determined by the clinician, based on all available information.

Potential Confounders

Age, gender, SES, birth weight, and race of the child were a priori considered as potential demographic confounders and included in analysis. In addition, self-report maternal and paternal ADHD symptoms, as derived from the Conners' Adult ADHD Rating Scale (Conners et al., 1999) and maternal alcohol use during pregnancy (yes or no) were considered as potential confounders.

Data Analysis

A regression analysis strategy, applying generalized estimating equations (GEE) (Diggle et al., 1994; Liang and Zeger, 1986), was used to estimate the effect of maternal and paternal smoking during pregnancy on children's ADHD-related behavior problems as rated by both parents and teachers simultaneously.

GEE, a statistical approach that allows the use of information from multiple informants, provides regression coefficients and their standard errors taking the correlation between ratings from parents' and teachers' reports into account (Horton et al., 2001). In this way, the potential bias because of either the parent or teacher was reduced and estimates were more efficient. We used the "unstructured" correlation as the covariance structure, which uses robust estimators of variances to protect against misspecifications of the covariance structure and to ensure the *p* values are not biased. Inattention and hyperactivity/impulsivity scores by maternal smoking status (yes or no), paternal smoking status (yes or no), and the interaction of the 2 were evaluated, with adjustment for potential confounders.

For binary diagnostic outcomes of ADHD, first, *chi square* analysis was conducted to evaluate the level of comorbidity between ADHD and ODD. Children were then divided in the 4 groups: a group with neither ADHD nor ODD (reference group), 1 with only ODD, 1 with only ADHD, and 1 with comorbid ADHD and ODD. This was followed by polytomous logistic regression analysis, using the Statistical Analysis System Categorical Model (CATMOD) (SAS Institute, 2001). The 4 diagnostic outcome groups served as outcomes and parental (maternal and paternal) smoking status as risk factors. This was followed by a model with additional confounders; child's age, gender, race, birth weight, parents' self-report ADHD symptoms, and maternal alcohol use during pregnancy. Both maternal and paternal smoking statuses were analyzed together in the same model.

RESULTS

Demographics

As shown in the first column of Table 1, children entered the current study when they were 3 or 4 (mean age = 4.31). The mean age for fathers was 33.58 and for mothers was 31.45, although there was a wide age range for both. Most families were "middle class," which was indicated by a mean SES score of 56.70 (Nakao and Treas, 1994). Approximately, a quarter of them were girls. The mean birth weight was relatively large (3293 g) in this sample,

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although 12.1% weighted less than 2500 g, i.e., low birth weight. The sample was racially diverse with 12% black, 10% Asians, and 18% mixed race.

There was no difference in the age of the children or their parents, proportion of girls, race/ethnicity, or birth weight by parental smoking status. However, children of parents who smoked during pregnancy came from families with a significantly lower SES and a much greater proportion of mothers from families where both parents smoked had drunk alcoholic beverages during pregnancy (63%). Mothers who smoked during pregnancy had greater ADHD symptom scores than mothers who did not smoke.

Maternal and Paternal Smoking During Pregnancy

During pregnancy, 33% of fathers and 18% of mothers smoked. Mothers and fathers had a significant concordance for smoking during pregnancy (odd ratio [OR] = 8.6, $p < 0.0001$), indicating that if the father smoked during his partner's (the mother's) pregnancy, she was over 8 times more likely to have smoked during that period.

Inattention and Hyperactivity/Impulsivity as a Function of Maternal and/or Paternal Smoking During Pregnancy

Figure 1, based on the GEE analysis shows behavioral score rating by teachers and parents evaluated simultaneously among the 4 parental smoking groups (neither parent smoked, only father smoked, only mother smoked, and both parents smoked). There were significant overall differences in inattention scores ($\chi^2(3) = 8.03$, $p = 0.045$), hyperactivity scores ($\chi^2(3) = 10.49$, $p = 0.015$), and total ADHD scores ($\chi^2(3) = 9.28$, $p = 0.015$). Post hoc pairwise comparisons showed that children in groups with maternal smoking (groups with only mother smoked or with both mother and father smoked) had significantly higher inattention ($p = 0.2$), hyperactivity ($p = 0.03$), and total ADHD ($p = 0.01$) scores than children in groups in which the mother did not smoke (i.e., neither parent smoked nor father only smoked).

Risks of ODD, ADHD, and Comorbid ADHD and ODD by Maternal and Paternal Smoking During Pregnancy

Table 2 shows the relationship of maternal and paternal smoking during pregnancy to risks for diagnoses of ODD, ADHD, and the 2 disorders comorbidity, first without covariates, then with adjustment of the confounder effects. Both maternal and paternal smoking statuses were included in the same model and the risk of being in one of the group relative to the reference group (neither parent smoked) was examined. Maternal smoking during pregnancy were associated with over a 5-fold increased risk (OR = 5.21, 95% confidence interval [CI] = 2.04–12.42, $p < 0.0001$) for comorbid ADHD and ODD, whereas paternal smoking had no notable influence (OR = 0.79, 95% CI = 0.11–3.57, $p = 0.40$). Similarly, maternal smoking during pregnancy were associated with over a 3-fold increased risk (OR = 3.76, 95% CI = 1.69–7.24, $p = 0.002$) for single morbid ADHD, whereas paternal smoking had no notable influence (OR = 0.67, 95% CI = 0.13–2.56, $p = 0.84$). However, maternal smoking was associated with an increased risk for ODD without ADHD. The significant association between maternal smoking and children developing ADHD alone (adjusted odds ratio [AOR] = 3.85, 95% CI = 1.30–11.10, $p = 0.014$) and comorbid ADHD and ODD (AOR = 4.10, 95% CI = 1.48–11.36, $p = 0.007$) remain significant even after controlling for the effects of potential confounders. When mother's and father's ADHD symptoms were added in the model, our findings still remained significant: ADHD alone (AOR = 4.00, 95% CI = 1.36–11.12, $p = 0.012$), and comorbid ADHD and ODD (AOR = 5.05, 95% CI = 1.47–12.50, $p = 0.001$).

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DISCUSSION

The current study evaluated the level of concordance for maternal and paternal smoking during pregnancy and examined whether maternal and paternal smoking during pregnancy is associated with elevated inattention and hyperactivity/impulsivity scores among preschool children as assessed by teacher and parent reports. Further, we examined whether maternal and paternal smoking during pregnancy is associated with an increased risk for ADHD, ODD or comorbid ADHD and ODD. Our data are consistent with, and expand results from, prior studies, providing 3 main findings. First, mothers were over 8 times more likely to have smoked during pregnancy if her partner smoked during her pregnancy. Second, negative effects of maternal, but not paternal, were documented with respect to ADHD symptoms. Third, children of smoking, as compared with children of nonsmoking, mothers were at an increased risk for developing comorbid ADHD and ODD, and ADHD alone, but not ODD alone. Father's smoking during pregnancy had no notable influence on diagnostic outcomes.

Potential damage to the fetus attributed to prenatal exposure to smoking in utero is widely recognized. Pregnant mothers are always advised by their obstetric care providers, and many times informally by friends and relatives, to give up smoking during pregnancy. Despite that, pregnancy has not proved to be an effective deterrent to smoking (Haug et al., 1994; Ockene, 1993). Prior research reported an association between smoking during pregnancy and maternal psychopathology such as depression, antisocial personality disorders and addiction, and maternal ADHD. To the extent that ADHD has been associated with smoking, this could be one of the compelling reasons why some mothers with genetic susceptibility for ADHD could not give up smoking during pregnancy despite the well-known risks to the fetus (Kollins et al., 2005). In our sample, there was a significant difference on maternal ADHD symptoms between mothers who smoked and mothers who did not (47.97 vs. 45.59, $p = 0.02$), although few mothers in each group had clinically significant ADHD symptomatology. Therefore, it is possible that the offspring of smoking mothers compared with non-smoking mothers have higher risk for ADHD because of both environmental and familial influences. However, to understand the effect of smoking during pregnancy as an environmental risk, the effect of both mothers and fathers ADHD symptom ratings, as derived from the Conners' Adult ADHD Rating Scale (Conners et al., 1999) were adjusted for in all of our analysis. Although paternal smoking was associated with an increased risk for maternal smoking during pregnancy (OR = 8.6, $p < 0.0001$), maternal, but not paternal, smoking was associated with elevated inattention and hyperactivity/impulsivity scores, as well as ADHD diagnosis and comorbid ODD in children. Taken together, associations between maternal smoking during pregnancy and elevated inattention and hyperactivity scores and the risk for ADHD (both comorbid with ODD and ADHD alone) appears to be due to the exposure to cigarette smoking in utero, independent of a familiar risk for ADHD.

Our study has methodological strengths. First, using multiple informants bring together ratings of behaviors across home and preschool environments, and offsets potential rating biases associated with each type of informant. Despite a tendency to treat teacher reports, rather than the parent reports, as the gold standard in developmental psychopathology research, the literature also suggests that children behave differently at home and at school (Woo and Rey, 2005). To maximize multiple informant data, we made novel use of an analytic strategy (GEE) that reduces informant bias by taking account of correlations between multiple informant reports. The analytic techniques combining mother and teacher reports produce more reliable measures, and lead to more precise estimates of the associations between parental smoking (the risk factor) and child behavioral problems (Richters and Pellegrini, 1989; Chilcoat and Breslau, 1997). Second, we had both

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dimensional measures of behavioral problems related to ADHD and DSM-based ADHD and ODD diagnoses ascertained by semi-structured psychiatric interviews. Final diagnoses were assigned to each child at the diagnostic consensus meeting.

Our study also has limitations. First, smoking is based on retrospective self-report, which is susceptible to threats to reliability and validity. Given the stigma against smoking during pregnancy, it is possible that smoking mothers, more so than smoking fathers, under-reported their smoking during pregnancy. Smoking mothers with a child who has behavioral problems may be more likely to look for reasons why their child has problems. This may cause them to report smoking during pregnancy more accurately than smoking mothers who had a child without behavioral problems. We incorporated both the mothers' and teachers' reports of inattention and hyperactivity/impulsivity in children to minimize potential reporter bias; however, prospective data on smoking or a measure of serum cotinine would have strengthened our findings greatly. Second, we do not have family history of ADHD, although we have measures of hyperactivity and inattention from the parents, and these effects were adjusted in all analyses. However, as the risk of smoking is known to be higher among those with ADHD than those without, it is possible that the associations between maternal smoking during pregnancy and the child's impairment in attention and increased risk for ADHD may be due to genetically correlated environmental risk (i.e., exposure to maternal smoking in utero which is higher among mothers with ADHD than mothers without ADHD). As we found no association between paternal smoking during pregnancy and child impairment and increased risk, we suggest that significant associations between elevated inattention scores and the risk for ADHD may be due to the fetus being exposed to an environmental toxin such as smoking. Ascertaining parents' lifetime ADHD status will significantly contribute to further clarification of this issue. Because the study is ongoing, we plan to collect a diagnosis of ADHD from parents and the clarification on parental ADHD status will inform our future studies.

Despite these limitations, the current study shows that maternal, but not paternal, smoking during pregnancy is associated with significantly higher inattention, hyperactivity, and total ADHD scores and with an elevated risk for ADHD (both comorbid with ODD and ADHD alone) among preschool children. Maternal smoking was not associated with ODD alone, but ODD is highly associated with ADHD (OR = 11.4, 95% CI = 6.0–21.6, $p < 0.0001$). It is therefore possible that maternal smoking is associated with ADHD, and that we observed the association between maternal smoking and ODD through its high correlation with ADHD. It is also possible that maternal smoking is associated with an increased risk for ADHD, and that, in turn, increases the risk for subsequent ODD. However, we need to be cautious about concluding that maternal smoking is primarily associated with an increased risk for ADHD, because a nonsignificant association between maternal smoking and ODD alone could be explained by lack of sufficient statistical power to detect the existing difference because of the small number of cases with only ODD. The current study has a primary focus on ADHD and therefore the sample size by itself does not allow us to test a role of maternal smoking on both ADHD and ODD. With a larger sample size, future studies may inform whether maternal smoking is a risk factor for both ADHD and ODD independently.

We had hypothesized that children of parents who both smoked would have the highest risk for behavioral problems. However, our data suggested that paternal smoking had no notable influence in behavioral problems: children of both parents who smoked and mother-only smoking had similar behavioral characteristics, and children in which neither parent smoked or only the father smoked also had similar behavioral characteristics. Moreover, parental smoking was not associated with any child outcomes (comorbid ADHD and ODD, ADHD alone, and ODD alone). Although we do not have a direct measure of postnatal smoking

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among parents, considering the addictive nature of smoking, it is likely that fathers who smoked during his partner's pregnancy were likely to continue smoking after the child was born. Therefore, while definitive understanding needs to wait for future studies and replications, we conclude that prenatal fetal exposure to smoking has a time-specific high toxic valence on offspring's optimal development.

Taken together, these findings suggest that maternal smoking during pregnancy represents a serious behavioral risk factor for ADHD in their offspring. As their partner's smoking had a striking influence on the risk of women indulging in the same risk behaviors during pregnancy, intervention for both mothers and fathers might be an effective means for preventing subsequent ADHD-related behavior, symptoms, and diagnosis in children. Developing a refined understanding is urgently needed to increase mothers' awareness of the risk of smoking during pregnancy to mitigate the long-term human and economic costs to children, their families, and society.

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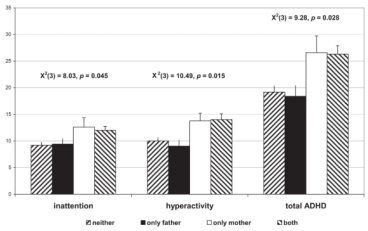

FIGURE 1.

Inattention, hyperactivity/impulsivity, and total ADHD scores as a function of maternal and paternal smoking during pregnancy. Differences in inattention, hyperactivity, and total ADHD scores among 4 groups of offspring by parental smoking status (nether parents smoked, only father smoked, only mother smoked, and both parents smoked) after controlling for age, gender, race, SES, birth weight, maternal drinking during pregnancy, mother's and father's ADHD symptoms. The reference group was offspring with neither parents smoked. Information provided by multiple informants (parents and teachers) was incorporated into the analysis.

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TABLE 1

Characteristics in Children of Nonsmoking and Smoking Parents

		Smoking Status					
	Total (*n* = 209) Mean (*SD*) [Range]	**1 Neither (*n* = 132) Mean (*SD*)**	**2 Father Only (*n* = 40) Mean (*SD*)**	**3 Mother Only (*n* = 10) Mean (*SD*)**	**4 Both Parents (*n* = 27) Mean (*SD*)**	**Overall Group Differences**	**Significant Pairwise Comparisons[a]**
Variable							
Child age (yr)	4.31 (0.47) [3.05–5.00]	4.30 (0.47)	4.00 (0.50)	4.19 (0.55)	4.36 (0.45)	$F_{3,205} = 0.34$, $p = 0.80$	—
Father's age (yr)	33.58 (6.83) [19–62]	33.69 (6.11)	33.45 (6.55)	33.90 (5.00)	33.15 (10.42)	$F_{3,200} = 0.06$, $p = 0.98$	—
Mother's age (yr)	31.45 (6.08) [17–44]	31.46 (5.86)	30.80 (6.58)	32.50 (6.40)	31.15 (6.36)	$F_{3,203} = 2.52$, $p = 0.86$	—
Family SES[b]	56.70 (14.36) [23.00–88.50]	59.28 (13.96)	52.63 (12.48)	50.56 (16.69)	51.38 (16.08)	$F_{3,203} = 3.47$, $p = 0.02$	1 <2,3,4
Birth weight (g)	3293 (704) [910–4593]	3555 (731)	3442 (524)	3401 (397)	3051 (845)	$F_{3,200} = 1.74$, $p = 0.16$	
Mother's ADHD symptoms[c]	45.54 (9.53) [30–90]	46.41 (8.73)	43.13 (6.79)	53.10 (8.14)	46.07 (6.35)	$F_{3,201} = 4.37$, $p = 0.005$	2 <3
Father's ADHD symptoms[c]	49.24 (11.26) [29–78]	49.66 (7.50)	48.62 (5.64)	50.00 (7.34)	47.85 (3.41)	$F_{3,201} = 0.70$, $p = 0.56$	
	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**		
Race							
White	124 (59.3)	75 (56.8)	25 (62.5)	7 (70.0)	17 (63.0)	$\chi^2(3) = 7.0$, $p = 0.09$[d]	
Black	26 (12.4)	17 (12.9)	4 (10.0)	1 (10.0)	4 (14.8)		
Asian	21 (10.1)	18 (13.6)	3 (7.5)	0	0		
Mixed and others	38 (18.2)	22 (16.7)	8 (20.0)	2 (20.0)	6 (22.2)		
Gender (girls)	54 (25.8)	32 (24.2)	10 (18.5)	2 (3.7)	10 (18.5)	$\chi^2(1) = 2.1$, $p = 0.55$[d]	
Alcohol use	45 (21.5)	18 (13.6)	7 (17.5)	3 (30.0)	17 (63.0)	$\chi^2(3) = 66.3$, $p < 0.001$[d]	1,2,3 <4

Bonferroni correction was applied for pairwise comparisons to account for multiple testing (The significance level was set at $p = 0.0083$).

N may differ slightly due to missing value.

[a] Numbers denote group numbers.

[b] Family SES was measured by Nakao and Treas (1994) taking both father's and mother's scores into consideration. The theoretical range goes from 0 to 100, with 50 to be in the middle. Higher scores denote higher SES.

[c] Parent's ADHD symptoms were measured by self-report using the Adult ADHD Rating Scale (Conners et al., 1999). Higher scores denote greater ADHD symptoms.

[d] Fisher exact test was applied.

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SES indicates socioeconomic status; ADHD, attention deficit hyperactivity disorder.

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TABLE 2

Rates of ADHD, ODD, and Comorbid ADHD and ODD by Parental Smoking During Pregnancy

	Nonsmoking *N* (%)	Smoking *N* (%)	OR (95% CI), *p*	[a] AOR (95% CI), *p*	[b] AOR (95% CI), *p*
Neither ADHD nor ODD (*N* = 88)					
Mother	82 (93.2%)	6 (6.8%)	Reference	Reference	Reference
Father	61 (70.1%)	27 (29.9%)			
Only ODD (*N* = 6)					
Mother	5 (83.3%)	1 (16.7%)	2.38 (0.30–18.52), *p* = 0.41	1.76 (0.17–20.00), *p* = 0.64	3.37 (0.22–38.46), *p* = 0.34
Father	6 (100%)	0	NE	NE	NE
Only ADHD (*N* = 65)					
Mother	52 (80.0%)	13 (20.0%)	3.76 (1.69–7.24), *p* = 0.002	3.85 (1.30–11.10), *p* = 0.014	4.00 (1.36–11.12), *p* = 0.012
Father	47 (72.7%)	18 (27.3%)	0.67 (0.13–2.56), *p* = 0.84	0.48 (0.15–2.17), *p* = 0.26	0.31 (0.06–1.92), *p* = 0.21
Comorbid ADHD and ODD (*N* = 50)					
Mother	33 (66.0%)	17 (34.0%)	5.21 (2.04–12.42), *p* < 0.0001	4.10 (1.48–11.36), *p* = 0.007	5.05 (1.47–12.50), *p* = 0.001
Father	26 (52.0%)	24 (48.0%)	0.79 (0.11–3.57), *p* = 0.40	0.75 (0.12–4.76), *p* = 0.76	0.85 (0.13–5.55), *p* = 0.86

Mother's and father's smoking history (nonsmoking vs. smoking) were analyzed simultaneously in the same model.

[a] Adjusted for gender, age, race and birth weight of the child, maternal drinking during pregnancy, and family SES.

[b] Adjusted for gender, age, race and birth weight of the child, maternal drinking during pregnancy, family SES, mother's ADHD symptoms, and father's ADHD symptoms. OR indicates odds ratio; AOR, adjusted odds ratio; NE, not estimable; ADHD, attention deficit hyperactivity disorder; ODD, oppositional defiant disorder.