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Is Maternal Smoking during Pregnancy a Causal Environmental Risk Factor for Adolescent Antisocial Behavior? Testing Etiological Theories and Assumptions

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Abstract

Background—Although many studies indicate that maternal smoking during pregnancy (SDP) is correlated with later offspring antisocial behavior (ASB), recent quasi-experimental studies suggest that background familial factors confound the association. The present study sought to test alternative etiological hypotheses using multiple indices of adolescent ASB, comparing differentially exposed siblings, and testing assumptions in the sibling-comparison design.

Methods—The study examined the association between maternal SDP and adolescent-reported ASB, criminal convictions, and membership in a group of individuals with early-starting and chronic ASB among 6,066 offspring of women from the National Longitudinal Survey of Youth, a representative sample of women in the United States. The analyses controlled for statistical covariates and examined associations while comparing differentially exposed siblings.

Results—At the population-level, each additional pack of cigarettes/day predicted greater mean adolescent-reported ASB symptoms (ratio of means=1.15, 95% CIs=1.08–1.22), odds of being in the top 10% of ASB (OR=1.34, 95% CIs=1.10–1.65), hazard of a criminal conviction (HR=1.51, 95% CIs=1.34–1.68), and odds of chronic ASB (OR=1.57, 95% CIs=1.25–1.99). SDP robustly predicted most assessments of ASB while controlling for measured covariates. When siblings exposed to differing levels of SDP were compared, however, all of the associations were attenuated and were not statistically significant: adolescent-reported mean ASB (ratio of means=0.86, 95% CIs=0.74–1.01), High ASB (OR=0.67, 95% CIs=0.41–1.12), criminal conviction (HR=0.98, 95% CIs=0.66–1.44), and Chronic ASB (OR=0.80, 95% CIs=0.46–1.38).

Conclusions—The results strongly suggest that familial factors account for the correlation between SDP and offspring adolescent ASB, rather than a putative causal environmental influence of SDP.

Most research on the association between maternal smoking during pregnancy (SDP) and offspring antisocial behavior (ASB) has been consistent with a causal inference (Ernst, Moolchan, & Robinson, 2001; Olds, 1997; Wakschlag, Pickett, Cook, Benowitz, & Leventhal, 2002). The causal inference has been supported recently by human research,

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including studies conducted across several countries (Brion, et al., 2010), controlling for numerous confounds (Paradis, Fitzmaurice, Koenen, & Buka, 2010), and that have explored differences in brain structure and functional processes in exposed and unexposed offspring (review in Derauf, Kekatpure, Neyzi, Lester, & Kosofsky, 2009). The results also are consistent with recent basic animal research on brain changes associated with prenatal nicotine exposure, including alterations in nicotinic acetylcholine receptors (e.g., Gold, Keller, & Perry, 2009).

Recent quasi-experimental studies in humans, however, have suggested that family background characteristics account for the statistical association between SDP and offspring ASB (review in Knopik, 2009). These studies, which use design features to rule out alternative hypotheses (Rutter, 2007; Shadish, Cook, & Campbell, 2002), suggest that unmeasured risk factors that covary with maternal SDP likely increase risk for ASB in the offspring instead of a direct prenatal environmental influence of SDP on risk for ASB.

Several studies on ASB have compared differentially exposed siblings by looking at risk for ASB among offspring where the mother changed her smoking across pregnancies. This design controls genetic and shared environmental factors that are confounded with SDP as alternative explanations for the apparent effect of SDP (Donovan & Susser, 2011; Lahey & D'Onofrio, 2010; Rutter, 2007). If the sibling who was exposed to greater SDP had higher levels of ASB (a within-family association), a causal association would be supported. In contrast, if both siblings had the same level of ASB, the results would suggest SDP does not cause ASB. Gilman, Gardner, & Buka (2008) found that differentially exposed siblings did not vary in their rates of childhood conduct problems. And, D'Onofrio et al. (2008) found that maternal SDP was not associated with increased risk for childhood conduct problems or oppositional problems when comparing differentially exposed siblings. A recent study found comparable results when exploring the association between SDP and offspring criminal convictions during adolescence and early adulthood (D'Onofrio, Singh, Iliadou, Lambe, Hultman, Grann, et al., 2010). These findings were confirmed in a novel in vitro fertilization study of maternal SDP and childhood conduct problems (Rice, et al., 2009), which controls genetic confounds by examining risk factors in women who were not genetically related to their children (Thapar, et al., 2007).

Certainly converging evidence across numerous studies and across various designs is necessary to support a causal inference (e.g., Rutter, Pickles, Murray, & Eaves, 2001). It is important to note that the existing quasi-experimental studies on ASB are limited by several problems. First, many of the studies are limited by measurement problems. Many studies relied on the same reporter (the mother) for the assessment of both SDP and ASB (Rutter, 2007). And, one study (D'Onofrio, Singh, Iliadou, Lambe, Hultman, Grann, et al., 2010) has been criticized for using extreme measures of ASB (criminal convictions), that may make the interpretation of findings difficult, if not impossible (Talati & Weissman, 2010). Second, a great majority of the studies are only based on childhood conduct problems, not ASB during adolescence when the societal costs and suffering associated with ASB are greater (e.g., R. Loeber, D. P. Farrington, M. Stouthamer-Loeber, & W. Van Kammen, 1998).

Third, the lack of measures of adolescent ASB also is problematic because SDP may differentially influence specific developmental trajectories of ASB. One study suggests that SDP may be more strongly associated with early-starting and chronic forms of ASB (Brennan, Grekin, & Mednick, 1999), which is consistent with the current theories suggesting that the trajectory of ASB is associated with early neurocognitive deficits (e.g., Moffitt, 2006). Fourth, few of the quasi-experimental studies have been able to test the assumptions inherent in their designs. For example, the sibling-comparison design has a number of limitations, including the inability account for whether exposure to the risk in one

pregnancy carries over to other pregnancies, historical changes, and factors that influence why women change their smoking behavior over time (Donovan & Susser, 2011; Lahey & D'Onofrio, 2010).

The current study sought to address these issues by: (a) examining the associations between SDP and multiple measures of ASB in a large study of offspring of a representative sample of women in the United States, (b) investigating these associations while comparing differentially exposed siblings with the same biological mothers, and (c) testing assumptions inherent in the sibling-comparison design.

Method

Sample

Mothers—The mother-generation for the current study was drawn from the National Longitudinal Survey of Youth 1979 (NLSY79). The NLSY79 was a nationally-representative household sample of 14–22-year-old male and female youth selected using a stratified and clustered design, with an oversample of African American and Hispanic youth (Baker & Mott, 1989). The NLSY79 sample consisted of the 4,926 females (1,472 African American, 977 Hispanic, and 2,477 non-Hispanic white and other groups) who have given birth to children.

Offspring—Biennial assessments of all biological offspring of all NLSY79 women began in 1986 (Chase-Lansdale, Mott, Brooks-Gunn, & Phillips, 1991). Participation in the 12 assessments through 2008 averaged >90%. Mothers answered questions about each of their children's behavior and environments in every assessment. Youth aged 10 years and over also reported on their behavior and environments in each assessment. A total of 11,506 offspring have been born to all of the women in the NLSY79 cohort through 2008. Observations were dropped from the current analyses if the observations were missing information about (a) the mother's identification number (n=11); maternal smoking during pregnancy (n=1,255), which was mostly due to an invalid skip pattern during a wave of assessment (D'Onofrio, et al., 2008); and adolescent ASB (n=5,010), which consisted mostly of offspring who were too young to be assessed for adolescent ASB. The analyses, therefore, were based on 6,066 offspring born to 2,694 mothers.

Measures

Maternal smoking during pregnancy—In every wave since 1986, CNLSY mothers were asked about their frequency of smoking during pregnancy for each pregnancy using a four-point scale. Information was obtained from the mother on birth outcomes and smoking and drinking during pregnancy in the first assessment following the child's birth. The frequency of maternal SDP is presented in Table 1. Using plasma biomarkers as the criterion variables, the validity of self-reported tobacco use during pregnancy has been demonstrated to be high in other studies (George, Granath, Johansson, & Cnattingius, 2006). Nonetheless, there is some systematic inaccuracy of false negatives (George, et al., 2006) and underestimating the amount of smoking (Post, Gilljam, Bremberg, & Galanti, 2008). The resulting imperfect sensitivity of self-reported smoking measures results in conservative tests of maternal smoking effects. The strongest evidence for the validity of maternal reports, however, is that they are consistently correlated with objective measures of the offspring's physical growth retardation (Day, et al., 1991). Previous CNLSY studies have found SDP to be highly correlated with offspring birth weight (D'Onofrio et al., 2008).

Offspring ASB

Adolescent-Reported ASB and High ASB: Across ages 14–17 years, youth completed a self-report questionnaire of ASB in private. They reported on 7 delinquent behaviors during the past 12 months from the Self-Reported Delinquency scale (SRD; Elliott & Huizinga, 1983): hurt someone badly enough to need bandages or a doctor; lied to parent about something important; took something from a store without paying for it; intentionally damaged or destroyed property that didn't belong to you; had to bring your parent(s) to school because of something you did wrong; skipped a day of school without permission; and ran away from home overnight. The SRD is the benchmark measure in contemporary delinquency research (R. Loeber, D. P. Farrington, M. Stouthamer-Loeber, & W. B. Van Kammen, 1998; Moffitt, Caspi, Rutter, & Silva, 2001). The 7 SRD delinquency items were selected for the CNLSY because they tap high-prevalence acts that are highly correlated with more serious delinquent behaviors. In three waves of the CNLSY, the young adult SRD delinquency scale also included 10 additional items. The 7-item scale delinquency correlated highly with the sum of the remaining more serious delinquency items, had good internal consistency, and showed excellent criterion validity in both sexes (Lahey, Van Hulle, D'Onofrio, Rodgers, & Waldman, 2008).

To create a measure of ASB we calculated a rounded average of the reported items across assessments from 14 to 17 years of age. The distribution of the self-reported ASB from 14–17 years of age is presented in Table 1. The distribution indicates that a majority of offspring report at least one item during the past year. In addition to of number of items reported in the previous year we also created an binary indicator of High ASB, which was based the highest 10% of the distribution of the SRD..

Criminal Convictions: Offspring also reported on their convictions for numerous offenses, including assault; robbery (using weapon or force); theft; fencing stolen goods; vandalism; other property offenses; marijuana possession; sale or distribution of marijuana; illicit drug possession; manufacturing, sale or distribution of illicit drugs; underage drinking; major traffic offense; or other crime. The offspring also reported the first age at conviction, which ranged from 10 to 30 years old. We predicted risk for ever being convicted, based on the first age of conviction. Kaplan-Meier estimates of the prevalence of criminal convictions revealed that 25.2% of offspring were convicted by the age of 30, with a higher prevalence in males (35.4%) than females (15.3%), which are consistent with national estimates (FBI, 2011).

Chronic ASB: To create an index of early-starting and Chronic ASB, we used a combination of mother-rated childhood conduct problems from 4 to 9 years old *and* adolescent self-reported ASB. Mothers rated childhood conduct problems using the Behavior Problems Index (BPI), a measure that selected items from the *Child Behavior Checklist* (Achenbach, 1978). The mean of the 7 BPI items indexed childhood conduct problems, and the items overlap substantially with those used to define child conduct problems in longitudinal studies (Fergusson & Horwood, 2002; Moffitt, et al., 2001). Previous studies have documented the factor structure and stability of the measure in the CNLSY, as well as the relation with maternal SDP (D'Onofrio, et al., 2008). To create a group of offspring with early-starting and chronic ASB we selected individuals who were in the top 20% on both measures. The measure was restricted to individuals with assessments at both time points (n=3,793), with 243 individuals (6.4%) meeting the criteria for Chronic ASB, which is generally consistent with recent epidemiological estimates (e.g., Barker & Maughan, 2009; Odgers, et al., 2008).

The measures of offspring ASB were highly associated with each other. Each additional item on the adolescent-reported ASB was associated with greater risk for criminal convictions (HR=1.56, $p<0.001$) and for membership in the Chronic ASB group (OR=2.94, $p<0.001$). High ASB (the top 10% of the self-reported ASB) was associated with more reported criminal convictions (HR=4.18, $p<0.001$) and with membership in the Chronic ASB group (OR=19.83, $p<0.001$).

Offspring-Specific Covariates—Table 2 describes the distribution of the covariates used in the study. To account for missing values in all of the covariates, we created dummy codes to compare any individuals with missing values to those observations with low risk. The study included a number of covariates that vary within families, including gender, offspring birth order, and maternal age at childbearing. Maternal age at childbearing compared teenage childbearing to non-teenage childbearing. High maternal alcohol consumption during pregnancy was also assessed, which was measured by reported drinking more than 3–4 days/month compared to those with less frequent consumption (D'Onofrio, et al., 2007).

Maternal/Familial Covariates—The analyses controlled for maternal reports of her history of adolescent delinquency (Rodgers, Rowe, & Li, 1994), which was indexed by comparing women in the top 10% to those in rest of the distribution. Low maternal intellectual abilities was based on the bottom 20% of the distribution of a composite score from the Armed Services Vocational Aptitude Battery, which was given in 1980. Low maternal educational attainment was assessed by fewer than 12 years of completed education. Low income was measured as familial income at the age of 30 below $5,795 in 1986 dollars (the bottom 10% of the distribution). The 1994 assessment included a detailed assessment of lifetime history of alcohol problems. The mothers were asked the number of binge episodes and a 25 item assessment of alcohol abuse and dependence items. If women ever reported binge drinking or any abuse of dependence items, they were considered to be at high risk for each measure. Maternal adolescent substance use was indexed by self report of any of the following substances during adolescence: cocaine, amphetamines, barbiturates, tranquilizers, psychedelic drugs, or heroin. Finally, we included family race/ethnicity, as measured by maternal self-report in the NLSY79 study, which included Caucasian, African American, and Hispanic groups.

Sampling weights—Based on clustered, unequal selection probability design, the NLSY79 provides weights indicating the inverse of the probability of each participant being selected into the sample. In family-based analyses, these weights apply equally to all CNLSY offspring to a given mother.

Analyses

Regression-Based Analyses—We used three models to examine the relation between maternal SDP and each measure of ASB. We fit the models in Mplus 6.11 (Muthén & Muthén, 1998–2010). Each model used robust standard errors at the original NLSY79 household level to account for the non-independence of the observations in extended-families, and each model used the sampling weights.

Model 1 predicted each measure of ASB by maternal SDP, offspring gender, and birth order. The parameter estimate associated with maternal SDP represents what we will refer to as the unadjusted association. Model 2 added all of the measured offspring-specific and maternal/familial covariates. The parameter associated with SDP quantifies the association of ASB to SDP while statistically controlling for the measured covariates. Model 3 predicted offspring ASB in the context of a fixed effects model at the mother level, which holds constant all

factors that siblings share (Allison, 2009). This model therefore compared differentially exposed siblings and thereby provided an estimate of the association between SDP and ASB while controlling for all familial factors—both genetic and environmental—that make siblings similar. The models were based on 1,088 offspring of 353 mothers who varied their smoking across pregnancies.

Because the distributions of the measures for ASB were different, the analyses used several analytical models. For offspring-reported adolescent ASB behavior counts we used negative binomial models to predict the mean number of ASB behaviors per person, a model that allows for over-dispersion of the response distribution relative to the Poisson (Long, 1997). We used logistic regression models to predict the dichotomous variables of High ASB and Chronic ASB. The negative binomial and logistic regression models were each based on a two level analysis with a random intercept at the second level to account for the clustering of siblings within a family. Finally because the reports of convictions were right-censored (the offspring had not lived through the entire risk period), we used Cox proportional hazards survival analysis models to predict first offspring criminal conviction. A sandwich estimator was used to account for the familial clustering in the survival analysis models.

Sensitivity Analyses—We ran additional analyses to test a number of moderators, rule out alternative explanation for the results, and examine some of the assumptions in the sibling-comparison design. First, we examined whether offspring gender and maternal alcohol consumption during pregnancy moderated the association between maternal SDP and offspring ASB. Second, we reran the analyses predicting each measure of ASB using a categorical assessment of maternal SDP (smoked or not during pregnancy) to examine whether any possible inaccuracy in reporting the amount of cigarette smoking could account for the results. Third, we ran the models without the sampling weights to determine the extent to which the use of sampling weights influenced the results.

Fourth, we tested a number of the assumptions in the sibling-comparison design, especially regarding the stable unit treatment value assumption—the assumption that exposure to the risk does not influence other unexposed participants (Rubin, 2006), which is particularly relevant for sibling-comparison designs (Lahey & D'Onofrio, 2010). If smoking in one pregnancy influenced all subsequent pregnancies, then a sibling-comparison approach would provide the wrong answer. Women who decrease their smoking over time may be quite different than those that increase their smoking during pregnancy. Furthermore, if the validity of the assessment of SDP has changed over time, the sibling-comparison approach could provide misleading results. To address these concerns, we ran a bi-directional case-crossover study (e.g., Meyer, Williams, Hernandez-Diaz, & Cnattingius, 2004) predicting adolescent-reported ASB in which we compared differentially exposed siblings among the first two children of women who either: (a) increased their smoking over time or (b) decreased their smoking over time. If the sibling-comparison parameters in both groups revealed no association, the results would suggest the findings from the overall sibling-comparison approach are robust to these assumptions.

Results

Regression-Based Analyses

Adolescent-Reported ASB—The parameter estimates and standard errors associated with each independent variable in the negative binomial models predicting adolescent-reported ASB are presented in Table 3. The SDP parameter estimates are reproduced in Table 4 as ratios of mean ASB behavior counts per person, with associated confidence intervals. In Model 1, each additional pack of cigarettes a mother smoked per day during pregnancy was associated with a 15% relative difference in mean ASB behaviors. When

controlling for all measured covariates, the results from Model 2 indicated that the association between SDP and ASB was attenuated (a 6% difference in ASB behaviors) but was still statistically significant. After fitting Model 3, the fixed effects (sibling-comparison) model that compared differentially exposed siblings, we found that the association went in the opposite direction (a negative 14% difference in ASB behaviors). Although the parameter was not statistically significant, the confidence interval excludes all ratios of means over 1.01, strongly suggesting that SDP does not lead to an increase in ASB. Taken as a whole, these analyses suggest that siblings have similar levels of ASB, regardless of level of exposure to maternal SDP.

High ASB—The parameter estimates associated with SDP for the other measures of ASB are presented in Table 4 (full results are available upon request). In Model 1, maternal SDP predicted increased odds (OR=1.34) of being in the highest 10% of the adolescent-reported ASB. In Model 2, which included statistical covariates, maternal SDP was not statistically associated with increased odds of High ASB (OR=1.08). In Model 3 (the sibling-comparison model), maternal SDP was not associated with High ASB (OR=0.67). Again, the estimate suggested decreased odds of High ASB, but was not statistically significant.

Criminal Convictions—In Model 1 a Cox proportional hazards model indicated that maternal SDP predicted increased risk (hazard) for being convicted of a criminal offence (HR=1.51). The inclusion of measured covariates in Model 2, attenuated the parameter estimate (HR=1.32), but the association was still statistically significant. The results of Model 3, the fixed effects (sibling-comparison) model, however, indicated no increased risk (HR=0.98) as a function of SDP. The results are consistent with the hypothesis that differentially exposed siblings have similar rates of criminal convictions.

Chronic ASB—The results of Model 1 indicated that maternal SDP predicted increased risk (OR=1.57) for having Chronic ASB. Maternal SDP robustly predicted Chronic ASB in Model 2 when statistical covariates were included the model (OR=1.31). Model 3 results indicated that the association between SDP and Chronic ASB went in the opposite direction but the parameter was not statistically significant (OR=0.80). Again, the results are consistent with the notion that maternal SDP is not associated with Chronic ASB when comparing differentially exposed siblings.

Sensitivity Analyses

First, the results indicated that neither offspring gender nor maternal alcohol consumption during pregnancy moderated the association between maternal SDP and offspring ASB, as measured by adolescent-reported ASB, while controlling for the measured covariates (full results available upon request).

Second, analyses predicting each measure of ASB using a dichotomous measure of SDP revealed comparable results. In the entire sample maternal SDP predicted adolescent-reported each measure of ASB The associations were somewhat attenuated but remained statistically significant when including the measured covariates. However, when comparing differentially exposed siblings the associations were greatly attenuated and were not statistically significant. Third, rerunning the analyses without the sampling weights provided comparable findings, indicating that the use of the sampling weights did not skew the results.

Fourth, we used a bi-directional, case-crossover approach that compared differentially exposed siblings in (a) women (n=185) who increased their smoking across their first two pregnancies (OR=0.83, CI=0.69–1.02) and (b) women (n=108) who decreased their smoking

across their first two pregnancies (OR=0.98, CI=0.70–1.37). Thus, SDP did not predict ASB in either group, and the difference (b_{logit}=.17, SE=.20, p=.40) was not statistically significant.

Discussion

The current study found converging evidence across all measures of ASB, including adolescent-reported counts of antisocial activities, membership in the highest 10% of ASB, criminal convictions, and membership in a group of individuals with chronic ASB across childhood and adolescence. Maternal SDP was robustly correlated with ASB in offspring during adolescence when statistically controlling for measured covariates, but when genetic and environmental factors that are correlated with SDP across families were controlled in sibling comparisons, no evidence was found for a casual influence of SDP on offspring ASB during adolescence.

The results and conclusions are consistent with previous quasi-experimental studies of child conduct problems (D'Onofrio, et al., 2008; Gilman, et al., 2008; Rice, et al., 2009) and provides converging evidence with previous research predicting offspring criminal convictions (D'Onofrio, Singh, Iliadou, Lambe, Hultman, Grann, et al., 2010). The results are also consistent with recent quasi-experimental studies of related constructs, including intellectual abilities and academic achievement (D'Onofrio, Singh, Iliadou, Lambe, Hultman, Neiderhiser, et al., 2010; Lambe, Hultman, Torrang, MacCabe, & Cnattingius, 2006; Lundberg, et al., 2010), different indices of ADHD (Lindblad & Hjern, 2010; Obel, et al., 2011; Thapar, et al., 2009), and psychiatric assessments of adolescent functioning (D'Onofrio, Singh, Iliadou, Lambe, Hultman, Grann, et al., 2010) and stress coping (Kuja-Halkola, D'Onofrio, Iliadou, Langstrom, & Lichtenstein, 2010). The conclusion also is consistent with recent studies that have found the associations between SDP and offspring cognitive and behavioral problems are confounded by measured familial risks (Batty, Der, & Deary, 2006; Boutwell & Beaver, 2010; Lavigne, et al., 2011; Roza, et al., 2009) when using extensive covariates and/or propensity score matching.

One strength of the current study was the opportunity to test some of the assumptions in the sibling-comparison design (Donovan & Susser, 2011; Lahey & D'Onofrio, 2010). The results of the bi-directional case-crossover approach suggest that carry-over effects of SDP from one pregnancy to another, possible changes in the validity of self-report SDP over time, or other historical changes do not unduly influence the interpretation of the sibling comparison results (also see Lundberg, et al., 2010).

Limitations

All quasi-experimental designs have threats to their internal and external validity (Shadish, et al., 2002). For example, the current study was not able to test every assumption in the sibling-comparison design, such as the specific generalizability of the findings from women who varied their smoking behavior across pregnancies to women without variability. We also did not explore the role of measurement error (review in Heath, et al., 1993), although the assessments of SDP and ASB have been shown to have excellent reliability.

Another statistical limitation of sibling-comparison designs is the reduction in power to detect associations because the estimates can only be based on the comparison of offspring of women who varied their smoking (Lahey & D'Onofrio, 2010), as is the case with all fixed-effects models (Allison, 2009). But, the lack of finding statistically significant associations with maternal SDP was not due solely to low statistical power. The confidence intervals around the SDP parameter predicting adolescent-reported ASB in the sibling-comparison models indicated the data is not consistent with the hypothesis that SDP causes

ASB. And, previous sibling-comparison analyses in the CNLSY have found that SDP is independently associated with offspring birth weight (D'Onofrio et al., 2008), which indicates that the use of the design with this dataset can detect small effects for some traits. Because the confidence intervals around the estimates from the sibling-comparison models predicting criminal convictions and chronic ASB are larger, however, the findings will need to be replicated in larger samples.

The current study also did not include all offspring of the NLSY79, as many of the offspring are not yet adolescents, but the analyses tried to account for this limitation by utilizing sampling weights. And, as is true for all regression analyses, there is the possibility that confounding variables masked a causal influence. In the sibling-comparison analyses such variables must (a) vary within families, (b) be positively associated with SDP, and (c) be negatively associated with ASB. Finally, the analyses do not identify the true causes of the association between SDP and offspring ASB because sibling comparison studies by themselves cannot identify the source of the familial confounding (Donovan & Susser, 2011; Lahey & D'Onofrio, 2010).

Given the limitations in the current study, research using other approaches, such as an in vitro fertilization design (Rice, et al., 2009), adoption studies (Leve, Neiderhiser, Scaramella, & Reiss, 2010), offspring of siblings and twins (D'Onofrio, et al., 2008), and larger sibling-comparison studies are required to test the causal inference regarding the association between SDP and offspring ASB and identify the confounding factors.

Implications and Directions for Future Research

Overall, the results of the current study failed to find evidence consistent with a causal prenatal environmental effect of SDP on offspring ASB. The current study addressed concerns that previous quasi-experimental studies relied on maternal reports for both SDP and ASB (Rutter, 2007) and predicted extreme measures of ASB that do not generalize (Talati & Weissman, 2010); in the current sibling-comparison analyses SDP did not predict either common forms of adolescent-reported ASB or rare indices of high ASB. In fact, we know of no quasi-experimental study of SDP that has shown an independent association between SDP and any measure of psychosocial, behavioral, or cognitive development (review Knopik, 2009). This suggests that previous human studies overestimated the causal influence of maternal SDP on ASB. It is important to stress that these findings are in contrast to the results of quasi-experimental studies of pregnancy related risks for which there is clear evidence consistent with a causal environmental effect (e.g., Cnattingius, 2004; Johansson, Dickman, Kramer, & Cnattingius, 2009).

The current results and the growing quasi-experimental research have important implications for many fields (D'Onofrio, Rathouz, & Lahey, 2011). More translational research is needed to understand the discrepant findings from quasi-experimental human research and experimental animal studies. Perhaps, biological differences in human and animal pregnancies (Huizink, 2009), such as mechanisms responsible for parturition (Mitchell & Taggert, 2009), account for some of the differences. Gene-environment interaction studies also must consider that SDP may not be an environmental causal influence. And, prevention efforts must seriously consider familial confounding--interventions may need to target the reduction in SDP *and* the familial risk factors that frequently co-occur with SDP.

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Table 1

Distribution of Maternal Smoking during Pregnancy and offspring Adolescent Antisocial Behavior

Variable	N	Percentage
Smoking during Pregnancy		
No packs/day	4431	73.1
Half packs/day	1205	19.9
One and a half packs/day	394	6.5
Two and a half packs/day	36	0.6
Adolescent ASB (rounded average number activities in past 12 months over ages 14—17 years)		
Zero	1562	25.8
One	2027	33.4
Two	1173	19.3
Three	675	11.1
Four[a]	365	6.0
Five[a]	168	2.8
Six[a]	70	1.2
Seven[a]	26	0.4

Note.

[a]Included in identifying a group of teenagers with High ASB.

Table 2

Distribution of Offspring-Specific and Familial Covariates

Variable	N	Percentage
Offspring-Specific Covariates[a]		
Female	2988	49.3
Birth Order		
One	2691	44.4
Two	1978	32.6
Three	931	15.4
Four plus	466	7.7
Maternal Teenage Childbearing		
No[c]	3514	57.9
Yes	2461	40.6
Missing	91	1.5
Maternal Alcohol Consumption during Pregnancy		
Low[c]	5540	91.3
High	516	8.51
Missing	10	0.2
Maternal/Familial Covariates[b]		
Mother Adolescent ASB		
Low[c]	2327	86.4
High	248	9.6
Missing	119	4.4
Maternal Intellectual Abilities		
High[c]	2077	77.1
Low	522	19.4
Missing	95	3.5
Maternal Educational Attainment		
High[c]	2614	97.0
Low	80	3.0
Maternal Income		
High[c]	2247	90.1
Low	247	9.9
History of Binge Drinking		
No[c]	2253	83.6
Yes	441	16.4
History of Alcohol Abuse/Dependence		
No[c]	2213	82.2
Yes	436	16.2
Missing	45	1.7
Maternal Adolescent Substance Use		

Variable	N	Percentage
No[c]	2076	77.1
Yes	578	21.5
Missing	40	1.5
Family Race/Ethnicity		
Caucasian[c]	1335	49.6
African American	832	30.9
Hispanic	527	19.6

Note.

[a]Based on 6,066 offspring.

[b]Based on 2,694 unique mothers.

[c]Used as the reference group in the analyses. Missing presents offspring or families with missing values for the variable.

Table 3

Regression Parameter Estimates (and Standard Errors) of Negative Binomial Models Exploring the Association between Maternal Smoking during Pregnancy and Adolescent-Reported Antisocial Behavior

	Model 1		Model 2		Model 3[a]	
Independent Variable	**b**	**SE**	**b**	**SE**	**b**	**SE**
Pack/day	0.14*	0.03	0.06*	0.03	−0.15	0.08
Female	−0.24*	0.03	−.25*	0.03	−.24*	0.03
Birth Order	0.01	0.02	−0.01	0.02	0.01	0.02
Maternal Teenage Childbearing						
No[b]			-	-		
Yes			0.25*	0.04		
Missing			0.20	0.14		
Maternal Alcohol Consumption during Pregnancy						
Low[b]			-	-		
High			0.00	0.05		
Missing			0.32	0.26		
Mother Adolescent ASB						
Low[b]			-	-		
High			0.08	0.05		
Missing			0.11	0.09		
Maternal Intellectual Abilities						
High[b]			-	-		
Low			−0.01	0.05		
Missing			−0.05	0.09		
Maternal Educational Attainment						
High[b]			-	-		
Low			0.08	0.08		
Maternal Income						
High[b]			-	-		
Low			0.10	0.06		

	Model 1		Model 2		Model 3[a]	
Independent Variable	**b**	**SE**	**b**	**SE**	**b**	**SE**
History of Binge Drinking						
No[b]			-	-		
Yes			0.08	0.04		
History of Alcohol Abuse/Dependence						
No[b]			-	-		
Yes			0.08	0.05		
Missing			0.09	0.12		
Maternal Adolescent Substance Use						
No[b]			-	-		
Yes			0.25*	0.04		
Missing			−0.10	0.16		
Family Race/Ethnicity						
Caucasian[b]			-	-		
African American			0.21*	0.06		
Hispanic			0.26*	0.04		

Note. All parameters are presented as log ratios of means.

*$p<.05$.

[a]Based on sibling-comparison model.

[b]Used as the reference group in the analyses. Parameters associated with the missing variables compared offspring with missing values on the covariates to those in the reference group.

Table 4

Relative mean ASB behaviors, odds of high and chronic ASB, and hazard of criminal conviction (and Confidence Intervals) for Offspring Antisocial Behavior associated with Maternal Smoking during Pregnancy for Three Analytical Models

Measure of ASB	Model 1	Model 2	Model 3
Adolescent Reported ASB[a]	1.15* (1.08 – 1.22)	1.06* (1.00 – 1.13)	0.86 (0.74 – 1.01)
High ASB[b]	1.34* (1.10 – 1.65)	1.08 (0.85 – 1.37)	0.67 (0.41 – 1.12)
First Criminal Conviction[c]	1.51* (1.34 – 1.68)	1.32* (1.16 – 1.49)	0.98 (0.66 – 1.44)
Chronic ASB[b]	1.57* (1.25 – 1.99)	1.31* (1.01 – 1.72)	0.80 (0.46 – 1.38)

Note. Parameters represent the relative increase in mean number of behaviors (for ASB), in odds of prevalent ASB (high or chronic), or in hazard of first criminal conviction associated with a mother smoking an additional pack per day.

[a]Based on a multi-level negative binomial model.

[b]Based on multilevel logistic regression model.

[c]Based on a multi-level survival analysis.