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A sibling-comparison study of smoking during pregnancy and childhood psychological traits

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Abstract

Prenatal exposure to substances of abuse is associated with numerous psychological problems in offspring, but quasi-experimental studies controlling for co-occurring risk factors suggest that familial factors (e.g., genetic and environmental effects shared among siblings) confound many associations with maternal smoking during pregnancy (SDP). Few of the quasi-experimental studies in this area have explored normative psychological traits in early childhood or developmental changes across the lifespan, however. The current study used multilevel growth curve models with a large, nationally-representative sample in the United States to investigate for potential effects of SDP on the developmental trajectories of cognitive functioning, temperament/personality, and disruptive behavior across childhood, while accounting for shared familial confounds by comparing differentially exposed siblings and statistically controlling for offspring-specific covariates. Maternal SDP predicted the intercept (but not change over time) for all cognitive and externalizing outcomes. Accounting for familial confounds, however, attenuated the association between SDP exposure and all outcomes, except the intercept (age 5) for reading recognition. These findings, which are commensurate with previous quasi-experimental research on more severe indices of adolescent and adult problems, suggest that the associations between SDP and developmental traits in childhood are due primarily to confounding factors and not a causal association.

Maternal smoking during pregnancy (SDP) is associated with numerous adverse outcomes in offspring, such as cognitive problems (Batty et al. 2006; Gilman et al. 2008) and criminal behavior (D'Onofrio et al. 2010; Brennan et al. 2002; Wakschlag et al. 2002). These associations are often attributed to the causal effects of teratogenic insults on the developing offspring (for reviews, see Wakschlag et al. 2002; Cornelius and Day 2009). Several lines of evidence support this causal inference, as animal models have suggested neural mechanisms (e.g., interference with cell proliferation and growth; Guerri 1998) by which neurodevelopmental effects may occur (Nordberg et al. 1991); dose-dependent effects have been found in which greater exposure is associated with more adverse outcomes (Huijbregts et al. 2008); and associations have been replicated across multiple samples (Cnattingius 2004; Wakschlag et al. 2006). Maternal SDP does not occur in isolation of other familial

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risk factors, however, and a causal relationship cannot be established until plausible alternative causes for these effects are ruled out (Rutter et al. 2001; Shadish et al. 2002).

Risk factors for offspring maladjustment that co-occur with maternal SDP include teenage motherhood (Ellingson et al. 2012), single-parent households (Ellingson et al. 2012), lower parental socioeconomic status (Monuteaux et al. 2006), lower levels of parental educational attainment (Gilman et al. 2008), parental externalizing traits (e.g., criminal behavior; Maughan et al. 2004), limited prenatal care (Cornelius et al. 2001), poorer parenting (e.g., poor supervision; Wakschlag et al. 1997), and marital instability (Wakschlag et al. 1997), to name a few examples. Further, maternal substance use during pregnancy is also influenced by genetic factors (i.e., the aggregate of small effects across many genes; Ellingson et al. 2012; Agrawal et al. 2008; D'Onofrio et al. 2003). Co-occurring environmental and genetic factors may, therefore, confound the association between maternal substance use during pregnancy and offspring functioning.

In addition to genetic and postnatal environmental risk factors, maternal SDP co-occurs with prenatal exposure to other drugs that also are associated with adverse offspring outcomes (for review, see Huizink and Mulder 2006). For example, prenatal alcohol exposure (PAE) is associated with psychological offspring outcomes, such as cognitive functioning (Mattson et al. 1997) and childhood externalizing outcomes (D'Onofrio et al. 2007; Disney et al. 2008). Although SDP co-occurs with use of other substances of abuse, many studies have not taken into account prenatal exposure to other substances when investigating the effects of maternal SDP in offspring. The need to account for such exposure is highlighted, however, by quasi-experimental studies on the effects of PAE (Gray et al. 2009), the results from which suggest that the associations between PAE and offspring functioning remain after controlling for specific confounds (e.g., parental externalizing behavior; Disney et al. 2008; Knopik et al. 2009) and general confounds (e.g., in a sibling-comparison study; D'Onofrio et al. 2007).

Most studies of SDP on offspring outcomes have controlled for specific, measured confounds (e.g., parental education) and have yielded robust, albeit significantly reduced, associations between SDP and psychological outcomes (Wakschlag et al. 2006; Wakschlag et al. 2010; Weissman et al. 1999). In contrast, quasi-experimental studies, which use design features to rule out confounding factors rather than statistical controls, suggest unmeasured confounds better explain the statistical associations between maternal substance use during pregnancy and offspring psychosocial problems (Knopik 2009; D'Onofrio et al. in press). For example, sibling-comparison studies, which compare siblings differentially exposed to maternal substance use during pregnancy (for a review of the sibling-comparison approach, see Lahey and D'Onofrio 2010) suggest that the statistical association between maternal SDP and cognitive functioning (Gilman et al. 2008; Lundberg et al. 2010; D'Onofrio et al. 2010), externalizing outcomes (Lindblad and Hjern 2010), delinquency (D'Onofrio et al. 2010; D'Onofrio et al. 2012), stress-coping (Kuja-Halkola et al. 2010), and other indices of adjustment are due to confounding factors, not the specific influences of SDP. Further, *in vitro* fertilization studies, in which mothers are not genetically related to the offspring but provide the prenatal and postnatal environments, also suggest that the association between maternal SDP and offspring conduct problems (Rice et al. 2009) and ADHD (Thapar et al. 2009) are due to confounding factors, notably genetic factors passed down from mothers to their offspring. The associations between SDP and pregnancy-related problems (e.g., birthweight) remain even when controlling for unmeasured familial confounds, however, suggesting that a direct, causal effect is present (Cnattingius 2004; Knopik 2009; D'Onofrio et al. in press).

Although quasi-experimental research has consistently failed to detect associations between SDP and offspring psychological outcomes after comprehensively controlling for familial confounds, this research is not without shortcomings (Talati and Weissman 2010). Of the family-controlled studies on SDP, most have focused on severe, discrete outcomes in offspring (e.g., 1% prevalence of violent criminal convictions); more common or normative outcomes have received little attention. In fact, we know of no quasi-experimental study that has studied the influence of SDP on the developmental trajectories of normative cognitive and psychological traits. It is, therefore, unclear whether the association between SDP and individual differences in normative and pathological outcomes (e.g., mild to moderate dysfunction; Trull and Durrett 2005) are similarly confounded by familial influences. In addition, previous quasi-experimental studies have typically focused on offspring outcomes in adulthood (e.g., criminal convictions, although see Gilman et al. 2008), and there may be direct effects of SDP on outcomes that are more proximal to prenatal exposure (e.g., early childhood) or on developmental changes in outcomes across childhood (D'Onofrio et al. 2012).

The current study seeks to address these shortcomings and aims to move the field forward in at least four important ways. First, we investigated the population-level associations of SDP with normative, continuous offspring psychological traits (temperament, cognitive functioning, externalizing outcomes) in the offspring of a large, representative sample of women in the United States. These outcomes are in contrast to the severe, discrete outcomes that previous studies of SDP have typically investigated. Notably, severe outcomes with low prevalences require large samples and greater power to detect effects and may miss meaningful, but subthreshold, dysfunction (Trull and Durrett 2005). Second, we used outcomes with repeated measures that spanned early childhood to early adolescence, which allowed for the investigation of individual differences in trajectories of offspring outcomes by using growth curve modeling (Meredith and Tisak 1990). Third, we statistically controlled for measured covariates to account for offspring-specific confounds. For instance, we statistically controlled for PAE, which co-occurs with maternal SDP and is associated with some psychological outcomes, even after controlling for unmeasured familial confounds. Finally, we used a sibling-comparison approach to investigate the association between SDP with offspring outcomes, while accounting for prenatal alcohol exposure and all unmeasured familial genetic and environmental factors that make siblings similar (D'Onofrio et al. in press; Lahey and D'Onofrio 2010; Donovan and Susser 2011).

Method

Participants

We analyzed data from the National Longitudinal Survey of Youth 1979 (NLSY79; Bureau of Labor Statistics and U.S. Department of Labor 2002), a nationally-representative sample that targeted 14-22 year olds (some of whom were siblings) in households of individuals in the U.S. workforce in 1979. An initial sample of 6,111 males and females not in the military were selected using a complex survey design. Eligible African-American and Hispanic youths were then oversampled, providing an additional 5,295 participants from these ethnic groups.

Beginning in 1986, the children of women in the NLSY79 were recruited and are referred to as the children of the NLSY (CNLSY). In the NLSY79, 4,930 female participants have given birth to 11,506 children involved in the CNLSY. Only children with data on SDP were included in the current study, which comprised 10,251 children (from the CNLSY) of 4,827 mothers (from the NLSY79) (see Table 1 for sample characteristics). The NLSY79 and CNLSY are multi-stage clustered samples (<http://www.NLSinfo.org>), as the NLSY79 was recruited in geographic clusters and both samples were recruited based on place of

residence. Offspring outcomes in the CNLSY were assessed every other year, and we grouped all measures in the current study into two-year periods to maximize sample coverage.

Measures

Maternal Smoking during Pregnancy—Maternal SDP was assessed within two years after childbirth and measured by self-reported mean number of packs smoked per day across the entire pregnancy. Participants responded as not smoking (zero cigarettes/day, 71%), smoking less than one pack per day (less than 20 cigarettes/day, 21%), one to two packs per day (20–40 cigarettes/day, 8%), and two or more packs per day (40+ cigarettes/day, <1%). We analyzed SDP as a continuous variable, consistent with previous studies using the CNLSY (D’Onofrio et al. 2012; D’Onofrio et al. 2008). Self-reported, retrospective reports of maternal SDP have been shown to be valid compared to self-reports during antenatal visits (Jacobson et al. 2002). Further, self-reported SDP during antenatal visits are remarkably consistent with bioassays (e.g., 94% agreement with serum cotinine levels; Lindqvist et al. 2002), however, we are aware of no data on the consistency of retrospective self-reports (used in the current study) with bioassays.

Cognitive Functioning—Five scales were used to measure cognitive functioning. The Peabody Picture Vocabulary Test-Revised (PPVT; Dunn 1981) was administered biennially from 3 to 12 years of age. The Math, Reading, and Reading Recognition subtests from the Peabody Individual Achievement Test-Revised (PIAT-R; Dunn and Markwardt 1970) were administered biennially from 5 to 14 years of age. Finally, the Digit Span subtest of the Wechsler Intelligence Scales for Children-Revised (WISC-R; Wechsler 1974) was administered biennially from 7 to 12 years of age. Adequate psychometric properties have been demonstrated for the PPVT (Costello and Faizunisa 1971), PIAT-R (Costenbader and Adams 1991), and Digit Span scale of the WISC-R (Irwin 1966; Rosenthal et al. 2006). All measures of cognitive functioning were standardized to have a mean of 100 and a standard deviation of 15.

Temperament—Maternal reports on the Children’s Behavior Questionnaire (CBQ; Rothbart et al. 2001), which contains subscales associated with a range of important outcomes (e.g., attachment predicts cortisol responses in certain stressful situations; Kertes et al. 2009), were used to measure temperament biennially, from 2 to 6 years of age. Three subscales were used to measure different domains of temperament (compliance, negative attachment, and sociability), and each subscale has demonstrated modest reliability in the CNLSY (Cronbach’s alpha coefficients ranged from 0.51 – 0.70; Baydar 1995). All measures of temperament were standardized ($M = 0$, $SD = 1$).

Externalizing Outcomes—Maternal reports on the Behavior Problem Index (BPI; Peterson and Zill 1986) were used to measure externalizing outcomes biennially from 4 to 13 years of age. The BPI is comprised of 16 items from the Child Behavior Checklist (CBCL; Achenbach 1978), which query the frequency of problem behaviors and are coded as 0 (never), 1 (sometimes), or 2 (frequently). The current study used 13 items from the BPI that cluster into factors indicating attention-deficit hyperactivity disorder (ADHD; three items), oppositional defiant disorder (ODD; three items), and conduct disorder (CD; seven items) (D’Onofrio et al. 2008). The BPI has demonstrated adequate reliability in the CNLSY across all ages for measuring ADHD ($\alpha = .67 - .74$), ODD ($\alpha = .69 - .76$), and CD ($\alpha = .68 - .80$) (Lahey et al. 2006).

Sum scores were computed for the items comprising each factor. That is, the maximum score for ADHD and ODD was six, and for CD it was 14. At the last wave of data

collection, the average score was 1.7 for ADHD ($SD = 1.5$), 2.1 for ODD ($SD = 1.6$), and 2.6 for CD ($SD = 2.4$).

Child- and Family-Level Covariates—Offspring sex and birth order and maternal age at birth were within-family covariates (i.e., specific to each sibling). Slightly more than half of CNLSY participants are male (51%). Of females in the NLSY79, 91% had three or fewer children in the CNLSY (1 child = 43%, 2 children = 33%, 3 children = 16%, 4+ children = 9%). The average maternal age at childbirth of CNLSY participants was 24.8 years old ($SD = 5.6$).

Offspring PAE was also assessed within two years after childbirth and was measured by self-reported days of drinking per week across the entire pregnancy. There were 3,182 (31%) offspring with PAE in the current study, of which the average exposure was about one-half drink per week ($M = 0.5$, $SD = 0.9$). In the total sample, the average exposure was 0.2 ($SD = 0.5$) drinks per week.

We included a number of between-family covariates (i.e., consistent across siblings). Ethnically, 53% of the mothers identified as Caucasian ($n = 6,097$), 28% as African-American ($n = 3,188$), and 19% as Hispanic ($n = 2,210$). Household income (i.e., income from all adults in the household) was reported for mothers at age 30 in 1986 inflation-adjusted dollars; maternal educational attainment was assessed as the total number of years of schooling; maternal intelligence was measured by a composite score of the Armed Services Vocational Aptitude Battery; and maternal delinquency was measured by symptom counts of the Self-Reported Delinquency Interview, taken at ages 15–22. Delinquency symptom counts were regressed on mother's age and standardized ($M = 0$, $SD = 1$) before analyses. See D'Onofrio et al. (2008) for more details concerning the covariates. Unfortunately, the CNLSY contains limited data on fathers, and family-level covariates were therefore limited to general-family (e.g., household income) or maternal-specific (e.g., delinquency) variables.

Sample Weights—Mothers in the current study were recruited for the NSLY79 in geographic clusters, with many participants in the NSLY79 coming from the same geographic location. Some members of the NSLY79 may, therefore, be similar due to geographical similarities (e.g., same neighborhood). To account for such similarities, probability weights at the NSLY79 household level were incorporated into all analyses to yield parameter estimates that are representative of all women in the United States. More details concerning the NSLY79 are available elsewhere (Baker and Mott 1989).

Data Analyses

Three multilevel, latent growth curve models were used to investigate whether SDP was associated with the first measurement and change across subsequent measurements for cognitive functioning, temperament, and externalizing outcomes (see Figure 1). That is, the intercept and slope in offspring outcomes were regressed on SDP and PAE, as well as child- and family-level covariates to statistically control for the influence of confounds. Including both maternal SDP and PAE in the same model allowed the effects of SDP to be isolated from PAE, as both are posited to exert effects via different routes.

There may be concern about the consequences of the non-normality of maternal SDP, as this measure is continuous and most mothers endorsed no SDP. The assumption of multivariate normality in multilevel modeling is flexible (e.g., Goldstein 2011, p. 28), however, and violation of this assumption results in a downward bias of standard error estimates *only* when large samples are not used (van der Leeden et al. 1997). We address potential concerns about normality for the specific measures of maternal SDP used in each model below.

Mplus, version 6 was used to estimate all parameters in models 1, 2, and 3 (Muthén and Muthén 2010). Because the NLSY79 and CNLSY are multi-stage clustered samples, models accounted for the clustering of data (i.e., the maternal household level). In addition, full-information maximum likelihood was used to handle missing values (Enders and Bandalos 2001). There were no adjustments made for multiple testing (e.g., Bonferroni correction), as these efforts would result in a more conservative analytic approach and the chief aim of the current study was to identify any possible effect of maternal SDP on offspring outcomes.

Model 1: General Associations—Model 1 estimated the effects of exposure to SDP (packs per day) on offspring outcomes at the sample level (i.e., without accounting for any familial confounds). This model accounted for within-family confounds (sex, birth order of offspring), including PAE (days drinking per week), but no between-family confounds (e.g., ethnicity and income).

Model 2: Accounting for Measured Covariates—Model 2 estimated the effect of exposure to SDP on offspring outcomes, while accounting for measured individual and familial confounds. Individual confounds (i.e., at the within-family level) included offspring sex, birth order, and maternal age at childbirth. Familial confounds (i.e., at the between-family level) included maternal household income, ethnicity, educational attainment, intelligence, and delinquency. In Model 1 and Model 2, we used a raw measure of maternal SDP (packs smoked per day), which was skewed (skewness=1.46, [skewness > 1.00 indicates a departure from normality]), suggesting these models may be biased towards finding associations between maternal SDP and offspring outcomes.

Model 3: Within-Family Exposure—Model 3 estimated the association between SDP with offspring outcomes within families (i.e., differential sibling exposure in a family). This approach accounts for familial factors that make siblings alike, so only within-family covariates (sex, birth order, maternal age at childbirth) were included in the model. To account for factors shared by siblings, two additional indices of SDP were constructed. To index general familial risk, the mean SDP (MSDP) for each mother across all pregnancies was calculated and entered at the between-family level (i.e., the average offspring exposure to SDP in each nuclear family). To index child-specific risk, the deviation of SDP (DSDP) exposure from general familial risk (i.e., MSDP) was calculated.

To illustrate this approach, consider a mother who curbed her smoking across three pregnancies, resulting in three children exposed to two packs, one pack, and no packs of SDP each day. Whereas the familial average of SDP exposure for these siblings is one pack (MSDP=1 for all children), the differential exposure to SDP within this family is different for each child. The first child has +1 differential exposure to SDP (DSDP=1), the second child has 0 differential exposure to SDP (DSDP=0), and the third child has -1 differential exposure to SDP (DSDP=-1) relative to his/her siblings. Thus, MSDP indexes between-family risk (i.e., familial risk relative to other families) and DSDP estimates the within-family risk (i.e., offspring risk relative to other siblings). To accurately estimate the within-family association for SDP, all of the offspring-specific covariates were similarly decomposed into their respective means and deviation scores. Models using these contrasts have been shown to provide accurate within-family (or sibling-comparison) estimates (Neuhaus and McCulloch 2006). This within-family measure of maternal SDP was not skewed (skewness=0.02), indicating that there were no biases on the associations of within-family effects of maternal SDP and offspring outcomes.

Of the 4,827 families in the current study, there was no exposure or no change in exposure to SDP and PAE across offspring (i.e., DSDP=0) in 66.0% of families. Of the remaining families with differential exposure to SDP across siblings (n=2,145, 34.0%), there were a

total of 1,684 participants in the CNLSY, with 1,068 exposed to less SDP and 992 exposed to more SDP than their sibling average.

Results

Cognition

Unstandardized regression coefficients of SDP predicting the intercept and slope for each outcome are displayed in Table 2. Maternal SDP was robustly associated with the intercept ($bs = -1.14$ – 2.36 , $ps = .01$) but not slope ($bs = -0.16$ – 0.17 , $ps = 0.12$ – 0.88) for all cognitive measures in Model 1. To put these effects into perspective, a one-pack increase in exposure to SDP was associated with a 2.36-point decrease in performance on the Reading Recognition subtest in the intercept (i.e., subtest performance at ages 4-5) but a non-significant increase in the slope (i.e., the trajectory of subtest performance through ages 13-14).

In Model 2, accounting for a set of specific, measured covariates attenuated most effects on cognitive measures. Only effects on the intercepts of Math ($b = -0.67$, $p = 0.03$) and Reading Recognition subtests ($b = -0.84$, $p = 0.01$) persisted, and, unexpectedly, the effect of SDP on increase in the slope of Reading Recognition reached statistical significance ($b = 0.24$, $p = 0.04$). That is, a one-pack increase in exposure to SDP was associated with a 0.24-point increase in performance on the Reading Recognition subtest at each subsequent wave following the intercept, after controlling for specific confounds.

Finally, by accounting for within-family differences to SDP exposure, nearly all associations were fully attenuated in Model 3. Only performance on the Reading Recognition subtest at the intercept ($b = -1.82$, $p < .01$) and on its trajectory ($b = 0.56$, $p = .01$) were associated with maternal SDP. The results suggest that SDP was independently associated with decreases in reading recognition when offspring are 4-5 years old, but SDP was also associated with an increase in reading recognition over time. To investigate whether multicollinearity between SDP and covariates could account for this effect in Model 3, post hoc analyses were conducted. These analyses estimated that multicollinearity accounts about 1.6% of the effect of SDP in Model 3 ($VIF=1.016$), indicating that multicollinearity is not the source of this unexpected effect.

Temperament

For temperament, associations between maternal SDP and maternal reports of offspring temperament were small ($bs = -0.03$ – 0.05) and few approached statistical significance ($ps = .09$ – $.89$) in Model 1. The intercept of attachment ($b = 0.05$, $p = .09$) and slope of compliance ($b = -0.03$, $p = .10$) were marginally significant but these effects were small in magnitude. In Model 2, effect sizes remained small ($bs = -0.03$ – 0.03) and statistical significance indicated reduced probabilities of true effects ($ps = 0.20$ – 0.80). In Model 3, associations generally increased in effect size ($bs = -0.11$ – 0.13) but few approached statistical significance ($ps = .07$ – $.69$). The intercepts of compliance ($b = 0.13$, $p = .07$) and sociability ($b = -0.11$, $p = .11$) were the only marginally significant effects in Model 3. Given that temperament measures were standardized, these results suggest that maternal SDP predicts, at most, one-tenth of a standard deviation change in offspring temperament at the intercept (ages 2-3).

Externalizing Outcomes

In Model 1, associations between maternal SDP and the intercept (i.e., age 4-5) of all externalizing outcomes were statistically significant ($ps < .01$) and medium in magnitude ($bs = 0.29$ – 0.33) relative to the variability in these outcomes ($SD = 1.5$ – 2.4). In addition, there

were small but marginally to statistically significant associations with the slope (i.e., change through age 13) for CD ($b = 0.04, p = .02$) and ADHD ($b = -0.02, p = .06$). In Model 2, associations between maternal SDP and the intercept (i.e., age 4-5) of externalizing outcomes remained statistically significant ($ps < .01$) but were slightly smaller than in Model 1 ($bs = 0.20 - 0.22$). In addition, there was a small effect that approached statistical significance for the slope of CD ($b = 0.03, p = .10$). Finally, in Model 3, the magnitude of effects were small and not statistically significant for either the intercept ($bs = -0.07 - 0.03, ps = .33 - .85$) or slopes ($bs = 0.00 - 0.03, ps = .34 - .92$) of externalizing outcomes.

Discussion

Although SDP is associated with most cognitive and externalizing offspring outcomes at the population-level, most associations in the current study were small to medium and did not reach statistical significance when comparing differentially exposed siblings. This is consistent with previous research (Knopik 2009; D'Onofrio et al. in press), which suggest that background familial factors associated with SDP explain the population-level associations between SDP and offspring outcomes. Only the intercept for reading recognition was associated with SDP in analyses that controlled for sibling exposure, however, analyses also showed a rebound from these initial delays (i.e., increased slope) in individuals exposed to greater SDP relative to his/her siblings. These effects, however, are based on statistical significance testing and could be due to type-II errors.

The current findings on cognitive measures are comparable to previous research on SDP and offspring outcomes. Batty and his colleagues (2006) used the CNLSY to examine the association between SDP and offspring performance on the PIAT-R (i.e., Math, Reading, and Reading Recognition subtests). Whereas the current analyses nested children within families to examine the effects of SDP on the intercept (i.e., at age 5) and slope (i.e., change through age 14) of offspring outcomes, Batty and his colleagues nested all assessments (i.e., assessments at ages 5-14) within offspring and nested offspring within families. Further, Batty and his colleagues adjusted for several measured confounds (e.g., maternal intelligence, education), similar to Model 2 in the current study, but did not adjust for all confounds that make siblings similar, as done in Model 3. Despite these differences, the two studies arrive at similar conclusions—confounds attenuated associations between maternal SDP and offspring performance on the PIAT-R.

Strengths

The current study benefited from the use of a large, nationally representative sample with repeated measures. First, these findings can be applied to the general United States population, including ethnic minorities (i.e., Hispanic, African-American families). Second, we used data from multiple offspring from the same family to conduct a strong quasi-experimental design, the sibling-comparison study. Third, we used repeated measures to conduct LGCMs to explore whether SDP was associated with initial levels of and/or change in offspring outcomes. Fourth, we used prospective data, which are more accurate than retrospective data. Fifth, analyses accounted for the effects of PAE, which co-occurs with maternal SDP and is posited to influence postnatal outcomes via different mechanisms than prenatal nicotine exposure. Finally, the current study examined associations between SDP and individual differences in a variety of continuous offspring outcomes, rather than relying on extreme indices of offspring developmental behavior.

Limitations

An important limitation of these findings is that they do not identify specific source(s) of the familial confounding between maternal SDP and offspring outcomes (Lahey and D'Onofrio

2010; Donovan and Susser 2011). Genetic and environmental factors, however, have been attributed to the covariation between maternal SDP and co-occurring risk factors (Ellingson et al. 2012), and genetic factors transmitted from mothers to offspring may explain the association between SDP and offspring academic functioning (D'Onofrio et al. 2010) and personality traits (Kuja-Halkola et al. 2010). In addition, many of the attenuated associations involving SDP and behavioral outcomes involve externalizing measures, which suggest that behavioral dysregulation (e.g., poor delayed gratification) also may be transmitted from parents to their offspring. Research in the fields of molecular genetics, quantitative genetics, neuroscience, and the social sciences will be needed to further the progress in this area.

Another limitation of the current study is the measurement of PAE. When assessing socially unacceptable behavior, the reliability and validity of self-reports are of concern (for review, see Gray et al. 2009; Henderson et al. 2007). Whereas maternal reports of SDP are reliable compared to bioassays, the psychometric adequacy of maternal reports of PAE are less certain. In addition, researchers have expressed concerns with using a single indicator for PAE (O'Leary & Bower, 2009); the current study used an item on the frequency of alcohol use, but the dose (i.e., quantity consumed) and timing of exposure are unknown. Future research investigating or accounting for PAE will need more detailed assessments.

Implications

The current study addressed the limitations of previous sibling-comparison studies of SDP in several ways. First, the study provided a rigorous, quasi-experimental analysis of the effects of maternal SDP on numerous indices of child adjustment in the offspring of a large, nationally-representative sample of women. We used a sibling-controlled design to control for familial confounds that may make siblings alike and statistical covariates to adjust for offspring-specific factors that could confound the associations between SDP and offspring development. Second, this study considered the full range of individual differences in multiple offspring outcomes, rather than focusing on severe, discrete outcomes, which require greater power to identify statistically significant associations. Supplementary analyses on birthweight, which is one of the most robust outcomes associated with SDP, yielded significant effects ($bs = -80.13 - 141.38$, $ps < .01$) and demonstrated adequate statistical power across all models. Finally, the current study investigated the association between SDP and the intercept and change of offspring outcomes by analyzing repeated measures in growth curve models.

The results of this study largely converge with previous quasi-experimental studies, which show familial confounds greatly attenuate associations between SDP and psychological outcomes. These findings provide strong evidence that familial factors are causing the intergenerational transmission of adverse outcomes in families in which offspring are exposed to SDP.

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Figure 1. Latent growth curve model of an offspring outcome, with the slope and intercept regressed on smoking during pregnancy and prenatal alcohol exposure

Latent growth curve model of an offspring outcome, with measurements from age 5-6 to 13-14, with the slope and intercept regressed on smoking during pregnancy (SDP) and prenatal alcohol (PAE) exposure. Including both SDP and PAE in the same model allowed the effects SDP to be isolated from PAE, as both are posited to exert effects via different routes. The estimates for the intercept and slope parameters are referenced by I and S, respectively. The estimates for the within- and between-family parameters are referenced by the $_{WI}$ and $_{BW}$ subscripts, respectively. The estimates for the SDP and PAE parameters are referenced by S and A subscripts, respectively. All models estimated within-family parameters on the intercept (I_{WIA} , I_{WIS}) and slope (S_{WIA} , S_{WIS}) and Model 3 also estimated between-family parameters on the intercept (I_{BWA} , I_{BWS}) and slope (S_{BWA} , S_{BWS}).

Table 1
Sample characteristics for the Children of the National Longitudinal Survey of Youth (CNLSY)

Maternal Variable	Sample Statistics ^a		
	n responding	n endorsing (%)	M (SD)
Child-Specific Variables (n=11,506)			
Smoking During Pregnancy (packs/day)	10,251	2,986 (29.1%)	0.38 (0.64)
Prenatal Alcohol Exposure (drinks/week)	10,232	3,184 (31.1%)	0.17 (0.54)
Sex (% Female)	10,251	5,038 (49.1%)	*
Birth Order	10,251	*	1.92 (1.10)
Maternal Age at Birth (years)	10,251	*	24.87 (5.63)
Mother-Specific Variables (n=4,930)			
Average Smoking During Pregnancy (packs/day)	4,827	1,640 (34.0%)	0.37 (0.59)
Average Prenatal Alcohol Exposure (drinks/week)	4,825	2,245 (44.5%)	0.17 (0.44)
Average Offspring Sex (% Male)	4,827	3,457 (71.6%)	*
Number of Children	4,827	*	2.22 (1.15)
Age at First Child Birth	4,827	*	22.92 (5.32)
Intellectual Ability (%)	4,581	*	39.90 (27.20)
Education (years)	4,827	*	14.00 (3.52)
Household Income (at age 30)	3,987	*	\$34,841 (\$38,913)
Delinquency (Reported in 1980)	4,552	*	0.00 (1.48)
Ethnicity (%)	4,827	*	*
Caucasian	*	2,752 (57.0%)	*
African-American	*	1,252 (26.0%)	*
Hispanic	*	823 (17.0%)	*

Note: In addition to the degree of maternal smoking during pregnancy and prenatal alcohol exposure, the percent of mothers endorsing any such exposure is provided (n endorsing). Delinquency is the number of delinquent activities during the previous year regressed on mother's age when she completed the Self-Reported Delinquency Interview. Intellectual ability was measured by a composite score of the Armed Services Vocational Aptitude Battery. Household income is measured as mothers reported net income at age 30, in 1986 inflation-adjusted dollars.

Table 2
Regression coefficients of smoking during pregnancy predicting the intercept and slope of offspring outcomes.

Outcome	Model 1 <i>f</i>		Model 2 <i>g</i>		Model 3 <i>h</i>	
	estimate (SE)	p-value	estimate (SE)	p-value	estimate (SE)	p-value
Vocabulary (PPVT) <i>a</i>						
Intercept	-1.17 (0.45)	0.01	-0.19 (0.45)	0.68	-0.34 (0.84)	0.69
Slope	-0.16 (0.13)	0.22	0.04 (0.14)	0.77	-0.03 (0.27)	0.92
Digit Span (WISC-R) <i>b</i>						
Intercept	-1.14 (0.37)	< .01	-0.32 (0.39)	0.41	0.27 (0.79)	0.73
Slope	-0.03 (0.21)	0.88	0.20 (0.22)	0.38	-0.17 (0.52)	0.74
Math (PIAT-R) <i>c</i>						
Intercept	-1.75 (0.30)	< .01	-0.67 (0.31)	0.03	-0.56 (0.58)	0.34
Slope	-0.01 (0.09)	0.88	0.12 (0.10)	0.22	0.05 (0.21)	0.83
Reading (PIAT-R) <i>c</i>						
Intercept	-1.62 (0.34)	< .01	-0.44 (0.36)	0.22	-0.36 (0.71)	0.62
Slope	0.08 (0.11)	0.49	0.12 (0.11)	0.29	-0.04 (0.23)	0.86
Recognition (PIAT-R) <i>c</i>						
Intercept	-2.36 (0.29)	< .01	-0.84 (0.3)	0.01	-1.82 (0.58)	< .01
Slope	0.17 (0.11)	0.12	0.24 (0.12)	0.04	0.56 (0.23)	0.01
Attachment <i>d</i>						
Intercept	0.05 (0.03)	0.09	0.01 (0.03)	0.77	-0.03 (0.07)	0.69
Slope	0.03 (0.02)	0.19	0.03 (0.02)	0.21	0.03 (0.05)	0.56
Compliance <i>d</i>						
Intercept	0.00 (0.03)	0.89	0.03 (0.03)	0.34	0.13 (0.07)	0.07
Slope	-0.03 (0.02)	0.10	-0.03 (0.02)	0.20	-0.07 (0.06)	0.20
Sociability <i>d</i>						
Intercept	-0.03 (0.03)	0.39	0.01 (0.04)	0.80	-0.11 (0.07)	0.11
Slope	0.03 (0.02)	0.24	0.01 (0.03)	0.67	0.07 (0.06)	0.25
ADHD (PBI) <i>e</i>						
Intercept	0.32 (0.04)	< .01	0.22 (0.04)	< .01	0.03 (0.08)	0.70

Outcome	Model 1 ^f		Model 2 ^g		Model 3 ^h	
	estimate (SE)	p-value	estimate (SE)	p-value	estimate (SE)	p-value
Slope	-0.02 (0.01)	0.06	-0.02 (0.01)	0.13	0.00 (0.02)	0.92
CD (PBI) ^e						
Intercept	0.33 (0.05)	< .01	0.21 (0.06)	< .01	0.02 (0.10)	0.85
Slope	0.04 (0.02)	0.02	0.03 (0.02)	0.10	0.02 (0.04)	0.70
ODD (PBI) ^e						
Intercept	0.29 (0.04)	< .01	0.20 (0.04)	< .01	-0.07 (0.07)	0.33
Slope	0.00 (0.01)	0.94	0.00 (0.01)	0.82	0.03 (0.03)	0.34

NOTE: All parameters were estimated with packs smoked per day as an indication of SDP.

- ^aIntercept is at age 3, slope measure change through age 12.
- ^bIntercept is at age 7, slope measures change through age 12.
- ^cIntercept is at age 5, slope measures change through age 14.
- ^dIntercept is at age 2, slope measure change through age 7.
- ^eIntercept is at age 4, slope measures change through age 13.
- ^fModel 1: SDP with within-family covariates (PAE, sex (female), birth order, and maternal age)
- ^gModel 2: SDP with between-family covariates
- ^hModel 3: With-family deviation of SDP from between-family mean of SDP exposure