9-1-2021

Dimension- and Context-Specific Expression of Preschoolers' Disruptive Behaviors Associated with Prenatal Tobacco Exposure

Suena H. Massey

Caron A.C. Clark

Michael Y. Sun

James L. Burns

Daniel K. Mroczek

See next page for additional authors

Authors

Suena H. Massey, Caron A.C. Clark, Michael Y. Sun, James L. Burns, Daniel K. Mroczek, Kimberly A. Espy, and Lauren S. Wakschlag

HHS Public Access
Author manuscript
Neurotoxicol Teratol. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:
Neurotoxicol Teratol. 2020 ; 81: 106915. doi:10.1016/j.ntt.2020.106915.

Dimension- and Context-Specific Expression of Preschoolers' Disruptive Behaviors Associated with Prenatal Tobacco Exposure

Suena H. Massey[1,2,3,*], **Caron A.C. Clark**[4], **Michael Y. Sun**[1,5], **James L. Burns**[2], **Daniel K. Mroczek**[2,3], **Kimberly A. Espy**[6,7], **Lauren S. Wakschlag**[1,2,3]

[1]Department of Psychiatry & Behavioral Sciences, Northwestern University Feinberg School of Medicine, 676 N Saint Clair St, Suite 1000, Chicago, IL, 60611 USA

[2]Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, 633 N Saint Clair St, 19th Floor, Chicago, IL, 60611 USA

[3]Institute for Innovations in Developmental Sciences, Northwestern University, 633 N Saint Clair St, 19th Floor, Chicago, IL, 60611 USA

[4]Department of Educational Psychology, University of Nebraska at Lincoln, 241 Teacher College Hall, Lincoln, NE, 68508 USA

[5]Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, NC, 27710 USA

[6]Department of Psychology, University of Arizona,1503 E University Blvd. Building 68, Tucson, AZ, 85724 USA

[7]Department of Psychiatry, University of Arizona, 1501 N Campbell Ave, Tucson, AZ, 85724 USA

Abstract

Objective—Precise phenotypic characterization of prenatal tobacco exposure (PTE) −related disruptive behavior (DB) that integrates nuanced measures of both exposures and outcomes is optimal for elucidating underlying mechanisms. Using this approach, our goals were to identify dimensions of DB most sensitive to PTE prior to school entry and assess contextual variation in these dimensions.

Methods—A community obstetric sample of *N*=369 women (79.2% lifetime smokers; 70.2% pregnancy smokers) from two Midwestern cities were assessed for PTE using cotinine-calibrated interview-based reports at 16, 28, and 40 weeks of gestation. A subset of *n*=244 who completed observational assessments with their 5-year-old children in a subsequent preschool follow-up

*Corresponding Author: suena.massey@northwestern.edu, Tel: 312-695-6479; Fax: 312-695-5010; Mobile: 312-282-2398.

Declaration of interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

study constitute the analytic sample. Using two developmentally-meaningful dimensions previously associated with emergent clinical risk for DB—*irritability* and *noncompliance*—we assessed children with 2 parent-report scales: the Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB) and the Early Childhood Inventory (ECI). We also assessed children by direct observation across 3 interactional contexts with the Disruptive Behavior Diagnostic Observation Schedule (DB-DOS). We used generalized linear models to examine between-child variability across behavioral dimensions, and mixed effects models to examine directly observed within-child variability by interactional context.

Results—Increasing PTE predicted increasing impairment in preschoolers' modulation of negative affect (irritability), but not negative behavior (noncompliance) across reported (MAP-DB) and observed (DB-DOS) dimensional measures. Moreover, children's PTE-related irritability was more pronounced when observed with parents than with the examiner. The ECI did not detect PTE-related irritability nor noncompliance.

Conclusions—Nuanced, dimension- and context-specific characterization of PTE-related DB described can optimize early identification of at-risk children.

Keywords

prenatal tobacco exposure; disruptive behaviors; oppositional defiant disorder; smoking during pregnancy; early childhood

1. Introduction

Disruptive behaviors (DB) are one of the earliest forms of psychopathology that, when progressive to severe antisocial behavior, are nearly always expressed before five years of age (Tremblay, 2010). In the Diagnostic and Statistical Manual of Mental Disorders (DSM), DBs, categorized as oppositional defiant disorder (ODD) and conduct disorder (CD), have traditionally been diagnosed using a symptom-based framework (APA, 2000). More recent neurodevelopmental models conceptualize DB *dimensionally,* in terms of problems with the modulation of irritability, behavior compliance, aggression, and low concern for others (Biedzio & Wakschlag, 2018; Wakschlag et al., 2018).

Prenatal tobacco exposure (PTE) has been associated with a variety of poor cognitive and behavioral outcomes in children, including, but not limited to, attention deficit hyperactivity disorder, conduct disorder, impaired learning and memory, and cognitive dysfunction (Knopik, 2009). More specific to the focus of this paper, PTE has also been robustly linked to DB in childhood (Corneluis, Natacha, & Nancy, 2011; Maughan, Taylor, Caspi, & Moffitt, 2004; Wakschlag & Hans, 2002) that appear to escalate into more severe antisocial behavior, including higher levels of arrests and substance dependence, by early adulthood (Fergusson, Woodward, & Horwood, 1998; Talati, Wickramaratne, Wesselhoeft, & Weissman, 2017). In this way, mechanisms that underlie the PTE-DB link are of critical public health importance.

The extent to which the PTE-DB link reflects direct teratologic effects (Knopik, 2009) versus confounding by individual and familial factors associated with maternal smoking during pregnancy (D'Onofrio et al., 2010; Roza et al., 2009; Wakschlag, Pickett, Cook Jr, Benowitz, & Leventhal, 2002) remains unclear. While quasi-experimental, genetically-informed designs using survey-based PTE measures support familial confounding and no teratologic effect (Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014), studies using in-depth, prospective, biologically-verified assessments of PTE do support direct teratologic effects (Clark, Espy, & Wakschlag, 2016; Eiden et al., 2015; Wiebe et al., 2015). Only one study to our knowledge, has combined a within-family design with prospective PTE assessment; here, a small, but significant, PTE-related effect was found (Estabrook et al., 2016). Another critical methodological gap concerns the developmental sensitivity of DB outcome measures in young children. High-quality outcome measures are critical to the accurate characterization of PTE-behavior pathways since normative misbehavior and DB are highly overlapping in early childhood (Clark, Massey, Wiebe, Espy, & Wakschlag, 2019). This methodologic challenge has received far less attention and constitutes the focus of the current investigation.

Early childhood is characterized by the development of self-regulatory and social skills necessary to meet heightened demands for behavioral autonomy as children enter the school environment (Biedzio & Wakschlag, 2018; Clark et al., 2019). Specific phenotypic markers in early childhood can differentiate normative misbehavior from severe and chronic problem behavior trajectories. For example, children with normative developmental trajectories exhibit a decline in aggression and tantrum behavior after two to three years of age (Shaw, Gilliom, Ingoldsby, & Nagin, 2003), while children with atypical trajectories, associated with chronic behavior problems, continue to demonstrate these symptoms with high frequency and intensity, including more hostile and forceful acts (Wakschlag et al., 2007). This aberrant trajectory of intensifying DB was evident in our previous independent study of toddlers with PTE (Wakschlag, Leventhal, Pine, Pickett, & Carter, 2006). Such findings underscore the importance of precise measurement of the *quality, pervasiveness, intensity, frequency, and context* of behavior when distinguishing clinically concerning DBs from normative misbehavior during this foundational early childhood period.

Behavioral checklists that are symptom-focused, aligned with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), and derived from measures for older children, such as the Child Behavior Checklist (Achenbach & Edelbrock, 1983) and the Early Childhood Inventory (Sprafkin, Volpe, Gadow, Nolan, & Kelly, 2002), are reliable and thus commonly-utilized tools in research on the PTE-DB link. However, there have been increasing calls for more nuanced, developmentally-based, dimensional approaches, including those that capture within-child variability in clinically-salient behaviors across different interactional contexts (Kaat et al., 2019). Specifically, differences in children's behavior when they are with parents versus teachers and other non-parental adults are clinically-meaningful and warrant consideration in diagnostic assessments (Dirks, De Los Reyes, Briggs-Gowan, Cella, & Wakschlag, 2012).

To address this need, we conceptualized a developmental framework and devised a suite of assessment tools for assessing core dimensions of DB in young children. This includes an observational assessment paradigm, the Disruptive Behavior - Diagnostic Observation System (DB-DOS) to capture typical and atypical behavior in response to frustration across varied interactional contexts (Wakschlag, Briggs-Gowan, et al., 2008; Wakschlag, Hill, et al.,

2008) and the Multidimensional Assessment of DB (MAP-DB), to capture parental reports of the frequency, quality and intransigence of children's behavior across a variety of everyday settings (Wakschlag et al., 2014). The combination of these multiple-informant, multi-dimension, cross-contextual measures creates a developmentally sensitive, empirically derived framework for capturing patterns of DB that deviate from the normative misbehavior of early childhood.

The goal of this study was to provide a dimension- and context-specific characterization of DB associated with a typical range of PTE in a community sample of preschool-aged children. Determination of the extent of PTE was based on a combination of maternal report and biological assays to provide a nuanced metric for lower levels of exposure typical of community-based samples. We focused on two manifestations of DB that also manifest as common normative misbehaviors and demonstrate substantial individual differences: directly-observed irritability (e.g. temper tantrums) and noncompliance (e.g., defiant and provocative behavior; Wakschlag et al., 2015). We predicted that a developmentally-sensitive approach would detect PTE-related impairment *not* detected by a DSM symptom–based approach, and would provide specification with respect to dimension, and interactional context.

2. Methods

2.1 Participants

Derivation of the analytic sample is illustrated in Figure 1. Women were recruited at either 16 (65%) or 28 weeks of gestation (35%), then assessed at 28 weeks and delivery for the Midwest Infant Development Study (MIDS) (N=369) using flyers distributed to all obstetric clinics in two Midwestern cities over a 4.5-year period. As the MIDS was designed specifically to examine the impact of prenatal tobacco exposure on infant regulatory processes, cigarette smoking was oversampled while women who endorsed illicit drug use or binge drinking (≥ 4 drinks per drinking occasion) at screening were excluded. At the time of the study, e-cigarettes were not available. Mothers did, however, report on their use of other forms of tobacco, including chewing tobacco, pipes, or cigars; only one mother reported smoking cigars. Non-smokers were broadly matched to smokers on demographic factors associated with cigarette smoking, i.e., educational attainment, race/ethnicity, and Medicaid status.

2.2 Procedures

As children approached their fifth birthdays, 345 eligible MIDS families were re-approached for participation in a preschool follow-up study (MIDS-P). Among the 299 mother-child dyads enrolled in MIDS-P, 244 mother-child dyads (121 boys, 123 girls) completed the lab-based observational assessment and constitute the analytic sample for this study. All of these dyads completed both a 1-hour home visit and a 3-hour laboratory assessment and had complete data necessary to calculate calibration-corrected exposure (see below; 89.4% of eligible dyads, 66.1% of the original MIDS birth cohort). Maternal race and ethnicity, education, and income in the analytic sample were not different from the original MIDS sample (Wiebe et al., 2015).

All women provided informed consent and were compensated up to $175 for participation in MIDS-P. All procedures in the MIDS and MIDS-P were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments and were approved by Institutional Review Boards at the University of Nebraska-Lincoln, the University of Illinois at Carbondale (MIDS) and Northwestern University (MIDS-P), respectively.

2.3 Measures

2.3.1 Prenatal Tobacco Exposure (PTE)—In the MIDS, smoking beginning one month prior to the last menstrual period through delivery, was assessed with timeline follow-back interviews (Sobell & Sobell, 1992) and bioassays at each prenatal visit (Wang, Tager, Van Vunakis, Speizer, & Hanrahan, 1997). During the TLFB interview, mothers also reported on their alcohol use during pregnancy. If mothers reported any alcohol use, we coded the child as alcohol exposed and controlled for this variable in the analyses. Cotinine, the major metabolite of nicotine, was quantified from maternal urine specimens collected at each prenatal visit with enzyme immunoassay and gas chromatography/mass spectrometry at the United States Drug Testing Laboratories. The PTE variable used in all analyses was a 'best estimate' of mean cigarettes/day derived from reported smoking from TLFB interviews, cotinine levels from bioassays of urine, and inter-individual variation in cotinine clearance (Dukic, Niessner, Benowitz, Hans, & Wakschlag, 2007; Dukic, Niessner, Pickett, Benowitz, & Wakschlag, 2009; Pickett et al., 2009).

2.3.2 Dimensions of Disruptive Behavior

2.3.2.1 Regulation of negative affect (irritability): Maternally-reported child *irritability*, the dispositional tendency to respond to blocked goal attainment with frustration and anger (Wakschlag et al., 2018), was quantified with an item response theory (IRT) score (Wakschlag et al., 2014, 2018) derived from the Temper Loss dimension of the MAP-DB (Wiggins et al., 2018). The MAP-DB is a 118-item parent questionnaire, with items rated on a 6-point scale from *never* to *many times a day*. Items in the MAP-DB focus on behavior across varied contexts, including with siblings, with parents, or when tired or upset, to provide a holistic understanding of children's behavior across these contexts. The Temper Loss scale comprises 22 items, such as "How often does your child keep on having a temper tantrum, fall out or meltdown even when you have tried to calm them down?"

Irritability was also derived from sub-dimensions of the Oppositional Defiant Disorder scale by summing specific items of the ECI in a manner consistent with prior work (Sprafkin et al., 2002; Stringaris & Goodman, 2009). Items on the ECI focus on DSM-based symptoms that are context-free, e.g. "loses temper" and rated on a 4-point scale from *never* to *very often*.

We also assessed irritability by direct observation, using the anger modulation dimension of the DB-DOS (Wakschlag, Briggs-Gowan, et al., 2008). Briefly, in the DB-DOS, children complete activities across 3 interactional contexts —with a non-parental adult who interacts with the child (*examiner engaged context*); with a non-parental adult who is present, but busy doing paperwork (*examiner busy context*); and with the child's parent (*parent context).*

Each of the contexts entails presses for frustration or non-compliance. For instance, in both of the examiner and parent contexts, children are asked to refrain from touching an attractive array of toys while the adult completes some paperwork. Children's behavior was rated by research assistants blind to maternal smoking information on 2 dimensions—anger modulation (irritability) and behavior regulation (noncompliance; 0 = No/negligible misbehavior; 1 = normative misbehavior, 2 = concerning behavior; 3 = clearly atypical behavior), across 3 interactional contexts; inter-rater weighted kappas = .45 – .75; intra-class correlation coefficients = 41– .71). Confirmatory factor analysis was used to derive scores that reflected each of the possible 6 dimension-by-context combinations (Cronbach's α = .73 to .91).

2.3.2.2 Regulation of behavior (noncompliance): Maternally-reported child *noncompliance*, the extent to which children respond to environmental limits and demands in a resistant, defiant and/or inflexible manner (Wakschlag et al., 2007), was quantified by an IRT score from the noncompliance dimension of the MAP-DB (Cronbach's α = .96). The noncompliance dimension comprises 22 items such as, "How often does your child act sassy, talk back or have a smart mouth?"

Noncompliance was further quantified using relevant ODD dimensions from the ECI (Stringaris & Goodman, 2009; Cronbach's α = .84). We also assessed noncompliance by direct observation using the behavior regulation dimension of the DB-DOS (Pickett, Wood, Adamson, D'Souza, & Wakschlag, 2008).

2.3.3 Covariates—To account for the impact of PTE-related socioeconomic risks on DB (Keenan & Wakschlag, 2002), we created a demographic risk index by allocating a point for each of the following factors, as measured during prenatal maternal interviews: unmarried, <high school education, and household income <$20,000 USD. We also controlled for the following maternal characteristics assessed in MIDS-P: antisocial behavior, measured with the Zoccolillo Antisocial Behavior Questionnaire (Zoccolillo, Tremblay, & Vitaro, 1996) (Cronbach's α=.75), symptoms of attention deficit-hyperactivity disorder (ADHD), quantified as a sum of items assessing ADHD from the Conners' Adult ADHD Rating Scale – Short Form (Conners, Erhardt, & Sparrow, 1999) ; Cronbach's α=.82) and depression symptoms, measured with the Center for Epidemiological Studies-Depression Scale 9-item version (Cheung, Liu, & Yip, 2007). Child-related covariates included age, male sex, and child I.Q., as measured with the Woodcock-Johnson Brief Intelligence Assessment – General Intellectual Ability Subscale (Woodcock, McGrew, & Mather, 2001). We also asked mothers to report whether or not their child had ever attended a preschool or kindergarten program or Head Start, as a measure of preschool attendance. The standardized family conflict scale score from the Family Environment Scale (Moos & Moos, 1987) provided an indication of children's exposure to conflict in the home. Material and financial hardship was assessed with the financial stressors scale from the Life Stressors and Social Resources Inventory (Moos & Moos, 1998). Finally, we asked mothers to report the total number of smokers residing in the child's home, including the mother if they still smoked, as an indicator of children's postnatal exposure to tobacco.

2.4 Data analysis

Prior to modeling, the distributions of all variables were inspected. For PTE (skewness = 4.02, kurtosis = 17.80), a square root transformation was used, as this form of transformation is more appropriate for addressing the multiple zero values attributable to non-smokers (Manikandan, 2010). All other variables followed normal distributions. For the DB-DOS and ECI maternal report measures of irritability and noncompliance, we utilized generalized linear models to attenuate problems related to heteroscedacity and ensure more robust standard errors.

Interactional contexts in the DB-DOS were analyzed as repeated measures using a linear mixed model for each DB dimension. The *examiner busy* context was coded as the reference context, so that estimates reflect deviations from the intercept for this context. This approach enabled us to estimate *between-child* effects of PTE on behavior, and *within-child* effects of interactional context on behavior. We compared several covariance structures using log likelihood difference tests, Akaike's Information Criterion, and the Bayesian Information Criterion, and found that a heterogeneous compound symmetry structure and a Toeplitz structure emerged as the best fitting covariance structures for irritability and noncompliance, respectively. DB-DOS context and covariates were entered into models first, followed by PTE, then the interaction terms PTE × context. Significant interactions ($p < .05$) were retained in the final models. Estimates of effect sizes for each model were obtained by squaring the correlation between the predicted and the observed values.

3. Results

Seventy-nine percent (79.2%) of participants reported having smoked cigarettes at some point in their lives. Based on the TLFB interviews alone, 58.8% of participants reported having smoked during pregnancy; our cotinine-adjusted estimate, however, suggested that this percentage was 70.2% (Table 1). The correlation between the cotinine-adjusted estimate of mean cigarettes/day and cotinine values ranged from $r = .52$ to .86, $p < .001$, while the correlation between the cotinine-adjusted estimate of mean cigarettes/day and the TLFB-reported mean cigarettes/day was $r = .45$, $p < .001$.

As shown in Table 2, PTE was associated with higher levels of MAP-DB irritability ($p = .02$, model pseudo $R^2 = .25$). That is, for each square root unit increase in PTE, the MAP-DB irritability score increased by 3.51, $p = .02$. Thus, a child whose mother smoked 1 cigarette per day on average would have a predicted irritability score of 24.08, whereas a child whose mother smoked 4 cigarettes per day would have a predicted score of 27.59, a little less than half a standard deviation above the mean. There was no significant relation of PTE to irritability symptoms from the ECI, however. Maternal ratings of noncompliance, as measured by both the MAP-DB and ECI showed no relation to PTE. Several covariates, including maternal symptoms of ADHD and child intellectual ability, were also significant in these models.

Next, as shown in Table 3, PTE-related irritability varied by DB-DOS interactional context. While there was no relation of PTE to observed compliance or irritability with the examiner, PTE was associated with anger modulation (irritability) specifically during the parent-child interaction context. This effect is illustrated in Figure 1, which shows dose-dependent PTE-related irritability in parent, but not examiner contexts (model pseudo R^2 = .05). Children without PTE showed stable levels of irritability across interactional contexts.

4. Discussion

Precise phenotypic characterization of PTE-related DB that integrates nuanced measures of both exposures and outcomes is needed to generate insights into underlying mechanisms. The combination of repeated, prospective, biomarker-calibrated assessments of PTE, and developmentally specific, multi-informant, cross-contextual observational assessments used in the current study provides novel support for dimensional and contextual specificity in PTE-related DB prior to school entry. Using these approaches, in this study, we found that observed PTE-related impairment in preschool aged children was *dimension-specific* (irritability but not behavioral non-compliance), and *context-specific* (with parents versus examiner).

4.1 Dimension specificity of PTE-related irritability

PTE-related disruptive behavior difficulties were specific to the regulation of negative affect (irritability) but not behavior (noncompliance). This pattern was replicated across maternal reports and direct observation and was robust to statistical control for multiple potentially confounding factors, including heritable markers of impairment in self-control (maternal antisocial behavior, maternal ADHD symptoms) and a range of sociodemographic risks. Children with high scores on *anger modulation* and *temper loss* dimensions of the DB-DOS and MAP-DB, respectively, demonstrate frequent and/or intensely dysregulated anger and frustration that builds rapidly, and is developmentally atypical for the given context (Grabell et al., 2017). When intense, pervasive, and persistent, these deficits and their neural substrates have been linked to stable, chronic patterns of externalizing behavior in non-clinical samples (Wiggins et al., 2018).

Importantly, while PTE has been widely linked to offspring irritability during childhood (Huijbregts, Warren, de Sonneville, & Swaab-Barneveld, 2008; Wakschlag et al., 2018; Wiebe et al., 2015) and adolescence (El Marroun et al., 2014), underlying mechanisms remain unclear. The association between maternal negative emotionality and persistent smoking during pregnancy (Eiden et al., 2011; Massey et al., 2016) for example, suggests the possibility of familial confounding. Since negative emotionality is a likely mechanism through which risk for substance use disorders is transmitted inter-generationally (Belcher, Volkow, Moeller, & Ferre, 2014), deeper mechanistic investigation via the specification of exposure-related phenotypes using the developmentally-sensitive approach described has important implications for prevention (Biedzio & Wakschlag, 2018).

The differential association of PTE with irritability rather than noncompliant behavior is inconsistent with our earlier work in which we examined an independent sample of toddlers. At 18 to 24 months of age, observed problems with *behavioral* rather than *emotional* regulation differentiated exposed from non-exposed children (Wakschlag et al., 2006). Meanwhile in the current cohort of preschool-aged children, PTE was associated with problems with *emotional* rather than *behavioral* regulation. Reasons for this discrepancy are unclear and could reflect differences between cohorts, classification of exposure, methodologic differences in the assessment of DB. The discrepancy could also reflect differences in the outward expression of frustration at 18 – 24 months versus at age 5 when PTE-related deficits in modulation of irritability under motivational contexts could be more readily observed. Regardless, clarifying and extending the relationship from PTE to affective versus behavioral dimensions of DB is recommended.

4.2 Contextual specificity and variability of PTE-related irritability

Beyond an expected association between PTE and irritability, we also observed a dose-dependent relationship between PTE and contextual variability in the inability to regulate frustration (Figure 1). Increasing PTE was associated with increasing difficulty in the modulation of irritability with parents relative to the examiner, consistent with other studies of young children's behavior across these same contexts (Frost, Jelinek, Bernard, Lind, & Dozier, 2018). DB-DOS contexts are specifically designed with motivational elements that increase the likelihood of strong negative affect and press for young children's capacity to regulate it. Young children with PTE did not show impairment in their capacity to modulate frustration with the non-parental examiner but did exhibit decrements during interactions with their mothers. Perhaps motivational elements are most powerful with familiar adults, when social inhibition is reduced. Indeed, across clinical, high-risk and community samples, young children typically show higher levels of misbehavior within the DB-DOS parent context relative to examiner contexts (Petitclerc et al., 2015). Further, consistent with the present findings, heightened irritability in parent, but not examiner contexts, has been associated with other early life adverse exposures (Frost et al., 2018).

Finally, when interactional contexts in the DB-DOS are viewed as different social environments, there is a possibility that prenatal exposure, like other forms of early adversity, could increase children's susceptibility to environmental conditions. Infants prenatally-exposed to cocaine exhibit greater negativity in response to socially salient stimuli (being held) but show *decreased* negativity in response to socially neutral stimuli (novel objects) (Locke et al., 2016). In the current study, PTE-related irritability may have been elevated with parents, who provide more socially salient stimuli relative to the examiner. Future studies examining how social salience influences contextual variation in the expression of exposure-related phenotypes are recommended.

4.3 PTE effects not detected with symptom-based measures

While both developmentally-specified, dimensional methods (MAP-DB, DB-DOS) detected the same pattern of differentiated PTE effects, this was not replicated with the symptom-based method despite our generation of irritable and noncompliant dimensions from the heterogenous DSM-based DB syndrome scores (Biedzio & Wakschlag, 2018; Stringaris & Goodman, 2009). Symptom-based assessments, which capture a narrower spectrum of extreme behaviors across multiple developmental time points, could be limited in sensitivity and specificity at the preschool age when normative misbehavior is common. Further, exposure effects may be expressed as risk patterns rather than frank disorders at this stage (Biedzio & Wakschlag, 2018).

Studies utilizing DSM-based approaches in young children constitute an important first step to establishing the clinical import of exposure related effects. However, as the field moves to a more neurodevelopmental, systematic approach, more nuanced dimensional approaches that assess contextual variability add specificity to enhance normal-abnormal differentiation in subtle exposure-related patterns in young children (Biedzio & Wakschlag, 2018). Combined with our prior work, the current study underscores the necessity of high-quality measurement—in both prenatal exposures (Estabrook et al., 2016) and in child outcomes (Clark et al., 2016). Developmentally-sensitive, context-specific assessments of child behavior across the first years of life are needed to specify which and how DB phenotypes, and their underlying substrates, evolve across developmental periods (Wakschlag et al., 2015; Wiggins et al., 2018).

Finally, a mean PTE of 10 cigarettes/day is commonly conceptualized as a threshold at which PTE-related externalizing problems are evident, though this convention is derived primarily from maternal reports of PTE in earlier decades (Stene-Larsen, Borge, & Vollrath, 2009).Though lifetime smoking and smoking during pregnancy were prevalent in our community-based sample (79.2% and 58.8%, respectively), only 2.5% of women smoked 10 or more cigarettes/day based on our cotinine-adjusted measure. Further, based on our integrated, cotinine-corrected PTE variable, mean PTE for the entire sample of children was 0.8 cigarettes per day (SD=2.3); 1.2 cigarettes/day (SD=2.7) among children with any PTE, and 4 cigarettes/day (SD=4.7) among children persistently exposed across gestation. These rates were somewhat lower than means based on maternal report alone and suggest that the robust validation of exposure based on cotinine may be essential for understanding a more nuanced effect. Notably, women in this sample were also screened carefully for other forms of substance use, allowing us to isolate specific effects of PTE even at relatively low exposure levels. Finally, the putative effects of PTE on child behavior are broad and not necessarily fully captured by our dimensional assessment approach.

4.4 Conclusion

In conclusion, results derived from high quality exposure measurement and dimensional, developmentally based assessments of variation across the DB spectrum may have enabled the detection of nuanced patterns not detectable in past studies that used general, symptom-based measurement approaches. Even subtle difficulties in PTE-related emotion regulation found in this study during the critical transition to the school environment, while not deterministic, could have compounding implications for children’s long-term socio-occupational success. Their detection yields an important opportunity for early prevention within a period of heightened neuroplasticity (Wakschlag et al., 2018).

Acknowledgements

This work was supported by grants R01DA014661 (PI K. Espy), R01DA023653 (MPI K. Espy, L. Wakschlag) and K23DA037913 (PI S. Massey) from the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (NIH). NIDA and the NIH had no role in the study design, data collection, analysis or interpretation of the data, or the decision to submit this manuscript for publication.

References

Achenbach TM, & Edelbrock CS (1983). Manual for the Child Behavior Checklist and Revised Behavior Profile. University of Vermont, Department of Psychiatry.

APA. (2000). Task Force on DSM-IV Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR. Washington, DC: American Psychiatric Association, 4.

Belcher AM, Volkow ND, Moeller FG, & Ferre S (2014). Personality Traits and Vulnerability or Resilience to Substance Use Disorders. Trends in Cognitive Science, 18(4), 211–217. Retrieved from 10.1016/j.tics.2014.01.010

Biedzio D, & Wakschlag LS (2018). Developmental emergence of disruptive behaviors beginning in infancy: delineating normal: abnormal boundaries to enhance early identification Handbook of Infant Mental Health. 4th ed. New York: Guilford.

Cheung YB, Liu KY, & Yip PSF (2007). Performance of the CES-D and its Short Forms in Screening Suicidality and Hopelessness in the Community. Suicide and Life-Threatening Behavior, 37(1), 79–88. doi:10.1521/suli.2007.37.1.79 [PubMed: 17397282]

Clark CAC, Espy KA, & Wakschlag LS (2016). Developmental pathways from prenatal tobacco and stress exposure to behavioral disinhibition. Neurotoxicology and teratology, 53, 64–74. doi:10.1016/j.ntt.2015.11.009 [PubMed: 26628107]

Clark CAC, Massey SH, Wiebe SA, Espy KA, & Wakschlag LS (2019). Does early maternal responsiveness buffer prenatal tobacco exposure effects on young children's behavioral disinhibition? Development and Psychopathology, 31(4), 1285–1298. doi:10.1017/S0954579418000706 [PubMed: 30428950]

Conners CK, Erhardt D, & Sparrow EP (1999). Conners' Adult ADHD Rating Scales (CAARS) Technical Manual.

Corneluis M, Natacha M, & Nancy L (2011). Effects of prenatal cigarette smoke exposure on neurobehavioral outcomes in ten-year-old children of teenage mothers. Neurotoxicology and teratology, 33(1), 137–144. [PubMed: 21256428]

D'Onofrio BM, Singh AL, Iliadou A, Lambe M, Hultman CM, Grann M, . . . Lichtenstein P (2010). Familial confounding of the association between maternal smoking during pregnancy and offspring criminality: a population-based study in Sweden. Archives of General Psychiatry, 67(5), 529–538. [PubMed: 20439834]

Dirks MA, De Los Reyes A, Briggs-Gowan M, Cella D, & Wakschlag LS (2012). Annual Research Review: Embracing not erasing contextual variability in children's behavior – theory and utility in the selection and use of methods and informants in developmental psychopathology. Journal of Child Psychology and Psychiatry, 53(5), 558–574. [PubMed: 22360546]

Dukic VM, Niessner M, Benowitz N, Hans S, & Wakschlag LS (2007). Modeling the relationship of cotinine and self-reported measures of maternal smoking during pregnancy: a deterministic approach. Nicotine & tobacco research, 9(4), 453–465. [PubMed: 17454700]

Dukic VM, Niessner M, Pickett KE, Benowitz NL, & Wakschlag LS (2009). Calibrating self-reported measures of maternal smoking in pregnancy via bioassays using a Monte Carlo approach. International journal of environmental research and public health, 6(6), 1744–1759. [PubMed: 19578458]

Eiden RD, Leonard KE, Colder CR, Homish GG, Schuetze P, Gray TR, & Huestis MA (2011). Anger, Hostility, and Aggression as Predictors of Persistent Smoking During Pregnancy. Journal of Studies on Alcohol and Drugs, 72(6), 926–932. [PubMed: 22051206]

Eiden RD, Molnar DS, Granger DA, Colder CR, Schuetze P, & Huestis MA (2015). Prenatal tobacco exposure and infant stress reactivity: role of child sex and maternal behavior. Developmental psychobiology, 57(2), 212–225. [PubMed: 25650169]

El Marroun H, Schmidt MN, Franken IHA, Jaddoe VWV, Hofman A, van der Lugt A, . . . White T (2014). Prenatal Tobacco Exposure and Brain Morphology: A Prospective Study in Young Children. Neuropsychopharmacology, 39(4), 792–800. doi:10.1038/npp.2013.273 [PubMed: 24096296]

Estabrook R, Massey SH, Clark CAC, Burns JL, Mustanski BS, Cook EH, . . . Wakschlag LS (2016). Separating family-level and direct exposure effects of smoking during pregnancy on offspring externalizing symptoms: bridging the behavior genetic and behavior teratologic divide. Behavior genetics, 46(3), 389–402. [PubMed: 26581695]

Fergusson DM, Woodward LJ, & Horwood LJ (1998). Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. Archives of General Psychiatry, 55(8), 721–727. [PubMed: 9707383]

Frost A, Jelinek C, Bernard K, Lind T, & Dozier M (2018). Longitudinal associations between low morning cortisol in infancy and anger dysregulation in early childhood in a CPS-referred sample. Developmental Sciences, 21(3), e12573. doi:10.1111/desc.12573

Grabell A, Li Y, Barker J, Wakschlag L, Huppert T, & Perlman S (2017). Evidence of Non-Linear Associations between Frustration-Related Prefrontal Cortex Activation and the Normal:Abnormal Spectrum of Irritability in Young Children. Journal of Abnormal Child Psychology, 46, 1–11. doi:10.1007/s10802-017-0286-5

Huijbregts SC, Warren AJ, de Sonneville LM, & Swaab-Barneveld H (2008). Hot and cool forms of inhibitory control and externalizing behavior in children of mothers who smoked during pregnancy: an exploratory study. Journal of Abnormal Child Psychology, 36(3), 323–333. doi:10.1007/s10802-007-9180-x [PubMed: 17924184]

Kaat AJ, Blackwell CK, Estabrook R, Burns JL, Petitclerc A, Briggs-Gowan MJ, . . . Wakschlag LS (2019). Linking the Child Behavior Checklist (CBCL) with the Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB): Advancing a dimensional spectrum approach to disruptive behavior. J Child Fam Stud, 28(2), 343–353. doi:10.1007/s10826-018-1272-4 [PubMed: 31452592]

Keenan K, & Wakschlag LS (2002). Can a valid diagnosis of disruptive behavior disorder be made in preschool children? American Journal of Psychiatry, 159(3), 351–358. [PubMed: 11869995]

Knopik VS (2009). Maternal smoking during pregnancy and child outcomes: Real or spurious effect? Developmental Neuropsychology, 34(1), 1–36. doi:10.1080/87565640802564366 [PubMed: 19142764]

Locke RL, Lagasse LL, Seifer R, Lester BM, Shankaran S, Bada HS, & Bauer CR (2016). Effects of prenatal substance exposure on infant temperament vary by context. Development and Psychopathology, 28(2), 309–326. doi:10.1017/S0954579415000504 [PubMed: 26037110]

Manikandan S (2010). Data transformation. Journal of Pharmacology and Pharmacotherapeutics, 1(2), 126–127. doi:10.4103/0976-500x.72373 [PubMed: 21350629]

Massey SH, Reiss D, Neiderhiser JM, Leve LD, Shaw DS, & Ganiban JM (2016). Maternal personality traits associated with patterns of prenatal smoking and exposure: Implications for etiologic and prevention research. Neurotoxicology and teratology, 53, 48–54. [PubMed: 26655208]

Maughan B, Taylor A, Caspi A, & Moffitt TE (2004). Prenatal smoking and early childhood conduct problems: testing genetic and environmental explanations of the association. Archives of General Psychiatry, 61(8), 836–843. [PubMed: 15289282]

Moos RH, & Moos BS (1987). The Family Environment Scale In Sherman R & Fredman N (Eds.), Handbook of Measurements for Marriage and Family Therapy (pp. 83–86). Philadelphia: Psychology Press.

Petitclerc A, Briggs-Gowan MJ, Estabrook R, Burns JL, Anderson EL, McCarthy KJ, & Wakschlag LS (2015). Contextual variation in young children's observed disruptive behavior on the DB-DOS: implications for early identification. Journal of Child Psychology and Psychiatry, 56(9), 1008–1016. doi:10.1111/jcpp.12430 [PubMed: 26095766]

Pickett KE, Rathouz PJ, Dukic V, Kasza K, Niessner M, Wright RJ, & Wakschlag LS (2009). The complex enterprise of modelling prenatal exposure to cigarettes: What is 'enough'? Paediatric and perinatal epidemiology, 23(2), 160–170. [PubMed: 19159402]

Pickett KE, Wood C, Adamson J, D'Souza L, & Wakschlag LS (2008). Meaningful differences in maternal smoking behaviour during pregnancy: implications for infant behavioural vulnerability. J Epidemiol Community Health, 62(4), 318–324. doi:10.1136/jech.2006.058768 [PubMed: 18339824]

Roza SJ, Verhulst FC, Jaddoe VW, Steegers EA, Mackenbach JP, Hofman A, & Tiemeier H (2009). Maternal smoking during pregnancy and child behaviour problems: the Generation R Study. Int J Epidemiol, 38(3), 680–689. [PubMed: 18775874]

Shaw DS, Gilliom M, Ingoldsby EM, & Nagin DS (2003). Trajectories leading to school-age conduct problems. Developmental Psychology, 39(2), 189–200. doi:10.1037/0012-1649.39.2.189 [PubMed: 12661881]

Skoglund C, Chen Q, D'Onofrio BM, Lichtenstein P, & Larsson H (2014). Familial confounding of the association between maternal smoking during pregnancy and ADHD in offspring. Journal of Child Psychology and Psychiatry and Allied Disciplines, 55(1), 61–68. doi:10.1111/jcpp.12124

Sobell LC, & Sobell MB (1992). Timeline Follow-Back In Litten RZ & Allen JP (Eds.), Measuring Alcohol Consumption: Psychosocial and Biochemical Methods (pp. 41–72). Totowa, NJ: Humana Press.

Sprafkin J, Volpe RJ, Gadow KD, Nolan EE, & Kelly K (2002). A DSM-IV– referenced screening instrument for preschool children: The Early Childhood Inventory-4. Journal of the American Academy of Child & Adolescent Psychiatry, 41(5), 604–612. [PubMed: 12014793]

Stene-Larsen K, Borge AIH, & Vollrath ME (2009). Maternal smoking in pregnancy and externalizing behavior in 18-month-old children: Results from a population-based prospective study. Journal of the American Academy of Child & Adolescent Psychiatry, 48(3), 283–289. doi:10.1097/CHI.0b013e318195bcfb [PubMed: 19242291]

Stringaris A, & Goodman R (2009). Three dimensions of oppositionality in youth. Journal of Child Psychology and Psychiatry, 50(3), 216–223. [PubMed: 19166573]

Talati A, Wickramaratne PJ, Wesselhoeft R, & Weissman MM (2017). Prenatal tobacco exposure, birthweight, and offspring psychopathology. Psychiatry research, 252, 346–352. [PubMed: 28327448]

Tremblay RE (2010). Developmental origins of disruptive behaviour problems: the 'original sin' hypothesis, epigenetics and their consequences for prevention. Journal of Child Psychology and Psychiatry and Allied Disciplines, 51(4), 341–367. doi:10.1111/j.1469-7610.2010.02211.x

Wakschlag LS, Briggs-Gowan MJ, Carter AS, Hill C, Danis B, Keenan K, . . . Leventhal BL (2007). A developmental framework for distinguishing disruptive behavior from normative misbehavior in preschool children. Journal of Child Psychology and Psychiatry, 48(10), 976–987. doi:10.1111/j.1469-7610.2007.01786.x [PubMed: 17914998]

Wakschlag LS, Briggs-Gowan MJ, Choi SW, Nichols SR, Kestler J, Burns JL, . . . Henry D (2014). Advancing a multidimensional, developmental spectrum approach to preschool disruptive behavior. J Am Acad Child Adolesc Psychiatry, 53(1), 82–96.e83. doi:10.1016/j.jaac.2013.10.011 [PubMed: 24342388]

Wakschlag LS, Briggs-Gowan MJ, Hill C, Danis B, Leventhal BL, Keenan K, . . . Carter AS (2008). Observational Assessment of Preschool Disruptive Behavior, Part II: Validity of the Disruptive Behavior Diagnostic Observation Schedule (DB-DOS). J Am Acad Child Adolesc Psychiatry, 47(6), 632–641. doi:10.1097/CHI.0b013e31816c5c10 [PubMed: 18434925]

Wakschlag LS, & Hans SL (2002). Maternal smoking during pregnancy and conduct problems in high-risk youth: a developmental framework. Development and Psychopathology, 14(2), 351–369. [PubMed: 12030696]

Wakschlag LS, Hill C, Carter AS, Danis B, Egger HL, Keenan K, . . . Briggs-Gowan MJ (2008). Observational Assessment of Preschool Disruptive Behavior, Part I: reliability of the Disruptive Behavior Diagnostic Observation Schedule (DB-DOS). J Am Acad Child Adolesc Psychiatry, 47(6), 622–631. doi:10.1097/CHI.0b013e31816c5bdb [PubMed: 18434926]

Wakschlag LS, Leventhal BL, Pine DS, Pickett KE, & Carter AS (2006). Elucidating early mechanisms of developmental psychopathology: the case of prenatal smoking and disruptive behavior. Child Development, 77(4), 893–906. doi:10.1111/j.1467-8624.2006.00909.x [PubMed: 16942496]

Wakschlag LS, Perlman SB, Blair RJ, Leibenluft E, Briggs-Gowan MJ, & Pine DS (2018). The Neurodevelopmental Basis of Early Childhood Disruptive Behavior: Irritable and Callous Phenotypes as Exemplars. American Journal of Psychiatry, 175(2), 114–130. doi:10.1176/appi.ajp.2017.17010045 [PubMed: 29145753]

Wakschlag LS, Pickett KE, Cook E Jr, Benowitz NL, & Leventhal BL (2002). Maternal smoking during pregnancy and severe antisocial behavior in offspring: a review. American journal of public health, 92(6), 966–974. [PubMed: 12036791]

Wang X, Tager IB, Van Vunakis H, Speizer FE, & Hanrahan JP (1997). Maternal smoking during pregnancy, urine cotinine concentrations, and birth outcomes. A prospective cohort study. Int J Epidemiol, 26(5), 978–988. doi:10.1093/ije/26.5.978 [PubMed: 9363518]

Wiebe SA, Clark CAC, De Jong DM, Chevalier N, Espy KA, & Wakschlag LS (2015). Prenatal tobacco exposure and self-regulation in early childhood: Implications for developmental psychopathology. Development and Psychopathology, 27(2), 397–409. [PubMed: 25997761]

Wiggins JL, Briggs-Gowan MJ, Estabrook R, Brotman MA, Pine DS, Leibenluft E, & Wakschlag LS (2018). Identifying Clinically Significant Irritability in Early Childhood. J Am Acad Child Adolesc Psychiatry, 57(3), 191–199.e192. [PubMed: 29496128]

Woodcock R, McGrew K, & Mather N (2001). Woodcock-Johnson Tests of Achievement . Itasca, IL. IL: Riverside Publishing.

Zoccolillo M, Tremblay R, & Vitaro F (1996). DSM-III-R and DSM-III criteria for conduct disorder in preadolescent girls: Specific but insensitive. Journal of the American Academy of Child & Adolescent Psychiatry, 35(4), 461–470. doi:10.1097/00004583-199604000-00012 [PubMed: 8919708]

Highlights

- Carefully controlled, genetics-informed studies report inconsistent findings regarding the causal nature of the prenatal tobacco exposure (PTE): disruptive behavior link.
- Methodological reliance on coarse, diagnostic checklists hinders a clear understanding of this link.
- Bioassay-corrected exposure measurement was combined with developmentally sensitive disruptive behavior measures tapping distinct clinical dimensions, informants and interactional contexts.
- PTE showed dose-dependent associations with preschool child irritability, but not behavioral noncompliance.
- Effects were present for developmentally-informed, but not clinical measures, and for mother-child, rather than examiner-child interactions.
- Nuanced, developmentally informed and context-sensitive measures are critical to the clear specification of PTE's effects.

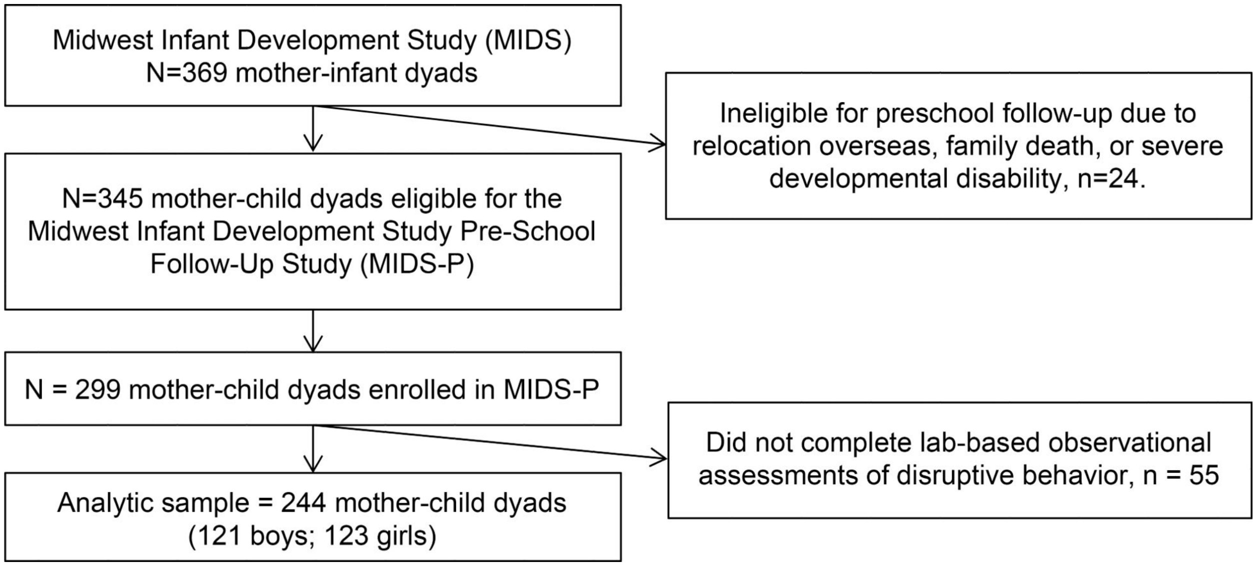

Figure 1.
Derivation of the analytic sample from the Midwest Infant Development Study (MIDS).

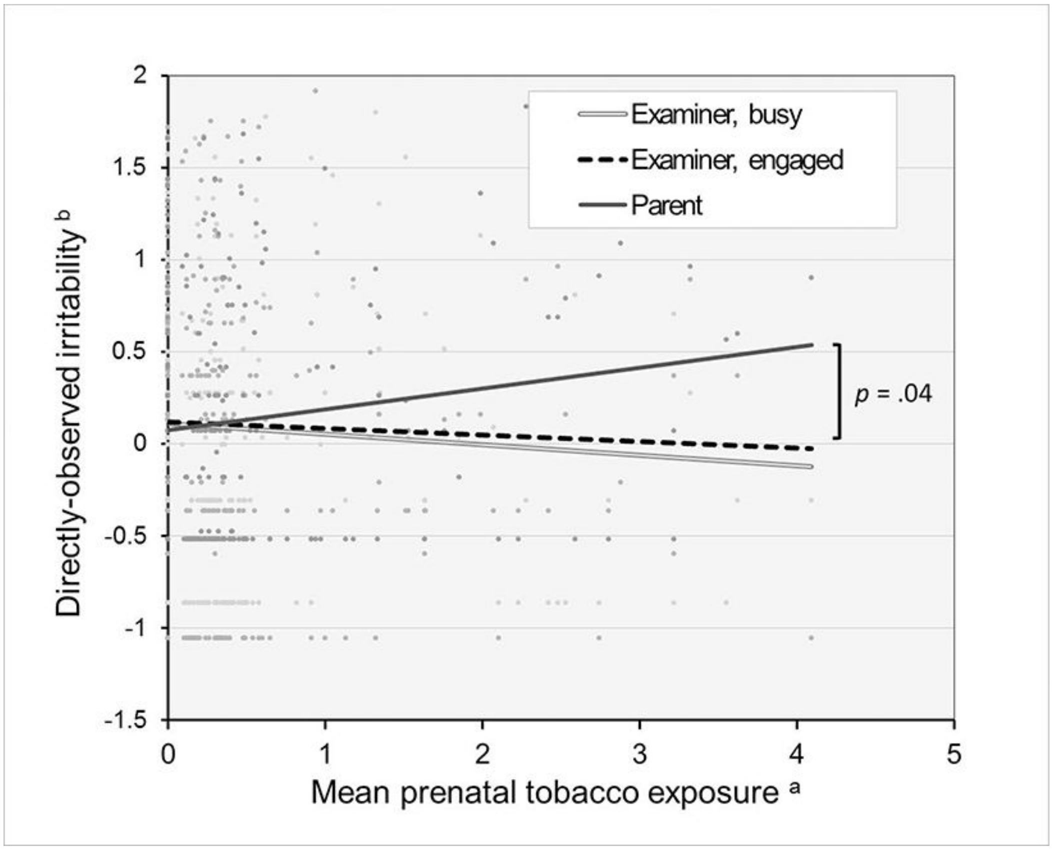

Figure 2.

Effect of increasing prenatal tobacco exposure [a] on within-child variability in directly observed irritability across three interactional contexts (examiner busy, examiner engaged, parent) [b] in non-referred preschoolers' (N=244)

[a] Mean calibrated cotinine-corrected cigarettes/day across pregnancy (square root transformed)

[b] Disruptive Behavior-Diagnostic Observational Schedule

Table 1.

Characteristics of mothers and preschoolers (N=244)

Maternal characteristics (during pregnancy)	Mean (SD) or %
Age (years)	30.94 (4.98)
Household income (USD)	$25,480 (20,263)
Unmarried	54.9%
Non-Hispanic Caucasian	84.8%
Completed < High school/GED	11.5%
Antisocial behavior [a]	2.65 (2.25)
Adult ADHD score [b]	45.21 (9.16)
Depression [c]	6.03 (5.10)
Any alcohol use during pregnancy (%)	38.1%
Nicotine dependence [d]	0.45 (.85)
Cigarettes/day [e]	0.84 (2.33)
0	29.5%
< 1	55.7%
1 – 5	9.0%
5 – 10	3.3%
> 10	2.5%
Child characteristics	
Age (in years)	5.07 (.26)
Male	49.6%
Intellectual ability [f]	98.36 (13.88)
Preschool/Head Start attender	60.2%
Family characteristics (at child follow-up)	
Family conflict [g]	44.93 (9.87)
Material hardship [h]	55.25 (8.93)
Household smokers	.77 (.84)

[a] Zoccolillo Antisocial Behavior Questionnaire

[b] ADHD Index score from the Conners' Adult ADHD Rating Scale – Short Form

[c] 9-item version of the Center for Epidemiological Studies-Depression Scale

[d] Modified Fagerstrom Test for Nicotine Dependence

[e] Mean cotinine-calibrated cigarettes/day across pregnancy

[f] Woodcock-Johnson Brief Intelligence Assessment, General Intellectual Ability Subscale

[g] Conflict scale from Family Environment Scale

[h] Financial stress scale from Life Stressors and Social Resources Inventory

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Predictors of preschoolers' disruptive behavior as reported by mothers using the Multi-dimensional Assessment of Preschool Disruptive Behavior (MAP-DB) and the Early Childhood Inventory (ECI) (N=244)

MAP-DB - *Irritability*	*Est (SE)*	*95% C.I.*	*Wald X^2*	*p*
Intercept	20.573 (2.344)	15.97 – 25.17	77.02	<.01
Child age	−.290 (.291)	−0.86 – .28	1.00	.32
Male sex	1.702 (1.938)	−2.10 – 5.50	.77	.38
Preschool attender	−2.014 (2.208)	−6.34 – 2.31	.83	.36
Child intellectual ability [a]	−.125 (.079)	−0.28 – .029	2.51	.11
Maternal antisocial behavior [b]	.128 (.626)	−1.10 – 1.36	.04	.84
Demographic risk index [c]	−.333 (1.143)	−2.57 – 1.91	.09	.77
Maternal ADHD symptoms [d]	.578 (.184)	.22 – .94	9.90	<.01
Maternal depression score [e]	.220 (.268)	−.31 – .75	.67	.41
Family conflict [f]	.259 (.110)	.04 – .47	5.56	.02
Material hardship [g]	−.044 (.114)	−.27 – .17	.15	.70
Prenatal alcohol exposure	2.036 (1.900)	−1.69 – 5.76	1.15	.28
Postnatal household smokers	−1.219 (1.244)	−3.66 – 1.22	.96	.33
Prenatal tobacco exposure [h]	3.506 (1.464)	.64 – 6.38	5.74	.02
MAP-DB - *Noncompliance*	*Est (SE)*	*95% C.I.*	*Wald X^2*	*p*
Intercept	23.712 (2.391)	19.03 – 28.40	98.38	< .01
Child age	−.474 (.291)	−1.04 – .10	2.66	.10
Male sex	3.756 (1.963)	−.09 – 7.60	3.66	.06
Preschool attender	−1.244 (2.137)	−5.43 – 2.95	.34	.56
Child intellectual ability	−.250 (.078)	−.40 – .10	10.33	< .01
Maternal antisocial behavior	.329 (.616)	−.88 – 1.54	.29	.59
Demographic risk index	−.769 (1.094)	−2.91 – 1.38	.49	.48
Maternal ADHD symptoms	.531 (.165)	.21 – .85	10.40	< .01
Maternal depression score	.252 (.246)	−.23 – .74	1.04	.31
Family conflict	.244 (.111)	.03 – .46	4.77	.03
Material hardship	−.178 (.103)	−.38 – .03	2.96	.09
Prenatal alcohol exposure	3.890 (1.952)	.07 – 7.72	3.97	.05
Postnatal household smokers	.909 (1.275)	−1.59 – 3.41	.51	.48
Prenatal tobacco exposure	1.654 (1.352)	−1.00 – 4.30	1.50	.22
ECI – *Irritability*	*Est (SE)*	*95% C.I.*	*Wald X^2*	*p*
Intercept	2.212 (2.252)	1.63 – 2.12	70.98	.27
Child age	−.023 (.030)	−.08 – .04	.56	.51
Male sex	.196 (.195)	−.18 – .58	1.02	.31
Preschool attender	.059 (.205)	−.34 −.46	.08	.77

Child intellectual ability	−.005 (.007)	−.02 – .01	.46	.50
Maternal antisocial behavior	.001 (.056)	−.11 – .11	< .01	.98
Demographic risk index	−.060 (.126)	−.30 – .18	.24	.63
Maternal ADHD symptoms	.050 (.015)	.02 – .08	10.97	< .01
Maternal depression score	.010 (.028)	−.04 – .06	.14	0.71
Family conflict	.026 (.011)	.01 – .05	6.03	0.01
Material hardship	−.010 (.012)	−.03 – .02	.56	0.45
Prenatal alcohol exposure	−.018 (.204)	−.42 – .38	< .01	0.93
Postnatal household smokers	−.021 (.134)	−.28 – .24	.02	0.88
Prenatal tobacco exposure	.195 (.153)	−.11 – .50	1.622	0.20
ECI – *Noncompliance*	*Est (SE)*	*95% C.I.*	*Wald X^2*	*p*
Intercept	4.336 (.394)	−3.59 – 5.14	122.66	< .01
Child age	.007 (.052)	−.10 – .11	.02	.89
Male sex	0.301 (.344)	−.37 – .97	.77	.38
Preschool attendance	−.106 (.349)	−.79 – .58	.09	.76
Child intellectual ability	−.037 (.015)	−.07 – −.01	6.61	.01
Maternal antisocial behavior	.045 (.086)	−.12 – .22	.28	.60
Demographic risk index	−.411 (.191)	−.78 – −.04	4.64	.03
Maternal ADHD symptoms	.069 (.025)	.02 – .21	7.57	< .01
Maternal depression score	.068 (.050)	−.03 – .17	1.81	.18
Family conflict	.053 (.018)	.02 –.09	9.22	< 0.01
Material hardship	−.010 (.019)	−.05 –.03	.28	.60
Prenatal alcohol exposure	−.284 (.344)	−.95 –.04	.68	.41
Postnatal household smokers	.028 (.215)	−.39 – .45	.02	.90
Prenatal tobacco exposure	.414 (.250)	−.08 – .90	2.75	.10

[a] Woodcock-Johnson Brief Intelligence Assessment, General Intellectual Ability Subscale

[b] Zoccolillo Antisocial Behavior Questionnaire

[c] Sum of single parenthood, < high school education, household income <$20 000 prenatally

[d] ADHD Index score from the Conners' Adult ADHD Rating Scale – Short Form

[e] 9-item version of the Center for Epidemiological Studies-Depression Scale

[f] Family Conflict scale from Family Environment Scale

[g] Financial stress scale from Life Stressors and Social Resources Inventory.

[h] Square root transformed mean cotinine-calibrated cigarettes/day across pregnancy

Table 3.

Predictors of preschoolers' directly observed problems with irritability and noncompliance in parent, examiner busy (intercept), and examiner engaged interactional contexts [a] (N=244)

	Dimension							
	Irritability				Behavior Regulation			
	Est (SE)	***95% C.I.***	***t***	***p***	***Est (SE)***	***95% C.I.***	***t***	***p***
Intercept (*examiner busy context*)	−.068 (.094)	−.25 – .11	−.72	.47	−.090 (.081)	−.25 – .07	−1.11	.27
Parent context	−.016 (.073)	−.16 – .13	−.22	.82	−.077 (.062)	−.20 – .04	−1.25	.22
Examiner engaged context	.027 (.082)	−.12 – .21	.33	.74	−.074 (.067)	−.21 – .06	−1.10	.27
Child age	−.008 (.012)	−.03 – .01	−.71	.48	−.026 (.011)	−.05 – −.01	−2.44	.02
Male sex	.185 (.070)	.05 – .33	2.64	<.01	.192 (.064)	.07 – .32	3.01	<.01
Preschool attender	.111 (.074)	−.03 – .26	1.50	.13	.182 (.067)	.05 – .31	2.71	<.01
Child intellectual ability [b]	−.007 (.002)	−.01 – .01	−2.71	<.01	−.007 (.002)	−.01 – −.01	−3.13	<.01
Maternal antisocial behavior [c]	−.009 (.017)	−.04 – .03	−.54	.59	−.014 (.016)	−.05 – .02	−0.90	.40
Demographic risk index	.056 (.041)	−.02 – .14	1.38	.17	.115 (.040)	.04 – .19	3.10	<.01
Maternal ADHD symptoms [d]	−.002 (.004)	−.02 – .01	−.33	.74	.006 (.004)	−.01 – .01	1.39	.17
Maternal depression score [e]	< −.001 (.008)	−.02 – .02	−.05	.96	−.008 (.007)	−.02 – .01	−1.03	.30
Family conflict [f]	.004 (.003)	−.01 – .01	1.14	.26	−.004 (.003)	−.01 – .01	−1.01	.31
Material hardship [g]	−.007 (.004)	−.02 – .01	−1.54	.13	−.008 (.004)	−.01 – −.01	−2.27	.02
Prenatal alcohol exposure	.062 (.075)	−.08 – .21	.83	.41	.065 (.068)	−.07 – .19	.95	.34
Postnatal household smokers	−.014 (.047)	−.10 – .08	−.29	.77	.033 (.043)	−.05 – 12	.77	.44
PTE [f]	−.066 (.070)	−.20 – .07	−.95	.34	.016 (.056)	−.10 – .13	.28	.78
PTE × *Parent context*	.160 (.078)	.01 – .31	2.04	.04	−.004 (.066)	−.14 – .13	−.07	.95
PTE × *Examiner engaged context*	.012 (.088)	−.16 – .19	.14	.89	−.041 (.073)	−.18 – .10	−.56	.57

Note: Estimates reflect divergence from the dimension score in the examiner busy (intercept) context for a child with average scores on covariates. For interpretability, all covariates were centered at the sample mean.

[a]Disruptive Behavior-Diagnostic Observational Schedule

[b]Woodcock-Johnson Brief Intelligence Assessment, General Intellectual Ability Subscale

[c]Zoccolillo Antisocial Behavior Questionnaire

[d]ADHD t score from the Conners' Adult ADHD Rating Scale – Short Form

[e]9-item version of the Center for Epidemiological Studies-Depression Scale

[f]Family Conflict scale from Family Environment Scale

[g]Financial stress scale from Life Stressors and Social Resources Inventory.

[h]Square root transformed mean cotinine-calibrated cigarettes/day across pregnancy