Published in final edited form as:

Matern Child Health J. 2012 April ; 16(3): 694–705. doi:10.1007/s10995-011-0766-0.

Long-term Effects of Prenatal Cigarette Smoke Exposure on Behavior Dysregulation Among 14-Year-Old Offspring of Teenage Mothers

Marie D. Cornelius,

Department of Psychiatry, Western Psychiatric Institute and Clinic, WPIC, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213, USA

Lidush Goldschmidt,

University of Pittsburgh Medical Center, 4415 Fifth Avenue, Webster Hall, Suite 138, Pittsburgh, PA 15213, USA

Natacha M. De Genna, and

Department of Psychiatry, Western Psychiatric Institute and Clinic, WPIC, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213, USA

Cynthia Larkby

Department of Psychiatry, Western Psychiatric Institute and Clinic, WPIC, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213, USA

Marie D. Cornelius: mdc1@pitt.edu

Abstract

In this prospective study, we examined the long-term effects of prenatal cigarette smoke exposure (PCSE) on behavioral dysregulation (BD) in the offspring of adolescent mothers. The adolescent mothers (mean age = 16; range = 12–18; 70% African American) were interviewed about their tobacco use during pregnancy. Offspring were followed to age 14 years (n = 318). Indices of BD outcomes included aggression, rule breaking, externalizing, social problems, attention, distractibility and activity. Multiple measures and multiple informants were used for each construct. Regression analyses were conducted to test if PCSE predicted the BD outcomes, adjusting for demographic and maternal psychological characteristics, and for prenatal exposure to other substances. Independent effects of PCSE were found. Exposed offspring had more aggressive, social, and externalizing problems on both the maternal report and the adolescent self-report measures. They were more active, had more attention problems and greater difficulty with distraction and task orientation. Most PCSE effects were found from first trimester exposure and from exposure to as few as 10 cigarettes per day. These results are consistent with previous findings in this cohort when offspring were 6 and 10 years old, demonstrating that the effects of prenatal cigarette smoke exposure can be identified early and persist into adolescence.

Keywords

Prenatal cigarette smoking; Behavior dysregulation; Teenage mothers; Adolescent offspring

Introduction

The rate of teenage pregnancy in the US remains significantly higher than in other developed countries [1], and it is estimated that one-third of all American girls will get pregnant by age 20. Smoking is common among pregnant adolescents; approximately 20–50% of pregnant adolescents smoke while only 10–15% of all pregnant women [2] and 15.6% of non-pregnant adolescents [3] are smokers. Using the most conservative estimate, if 20% of the 435,427 girls aged 15–19 who gave birth in 2006 [4] smoked while they were pregnant, at least 87,085 American infants were exposed to gestational tobacco from these teenage pregnancies alone. The health of these children is compromised by prenatal cigarette smoke exposure (PCSE), which has been associated with multiple adverse outcomes in offspring [5–17]. However, despite the high prevalence of smoking among pregnant teenagers, the level or quantity of smoking among pregnant teenagers is lower than that found in pregnant adults [7, 18], therefore long-term effects on the offspring are unknown.

PCSE affects central nervous system (CNS) development predisposing the offspring to neurobehavioral deficits, measured as irritability or difficult temperament during infancy and poor self-regulation during childhood [11]. PCSE is consistently associated with neuropsychological effects on behavior such as hyperactivity [10, 19–24] and attention deficits [5, 23]. PCSE also predicts other difficulties in self-regulation, such as aggressive behavior [10, 12, 21, 22, 24–29] and conduct problems in childhood [30–33] and adolescence [34, 35]. Studies of PCSE using prospective designs and statistical control for confounders [11, 36] show that PCSE is independently associated with offspring aggressive [10, 37, 38] and antisocial behavior [24, 35, 39]. However, no prior study has examined the relation between PCSE and these outcomes in the adolescent offspring of teenage mothers.

Hyperactivity, inattention and externalizing behavior including aggression can be viewed as manifestations of the construct referred to as behavior dysregulation [40]. Animal models suggest a plausible mechanism for the neuroteratogenic influence of nicotine on the fetus. Nicotine provokes alterations in neural cell replication leading to deficits in synaptic neurochemistry [39, 41] and resulting in BD. Other factors can lead to neurobehavioral deficits in human offspring, and women who smoke during pregnancy are more likely to exhibit these risk factors, including psychopathology [38], low SES [16], and use of other substances during pregnancy [8, 42, 43]. Therefore, it is important to control for demographic factors, maternal psychopathology and other prenatal substance exposures when testing for teratological PCSE effects.

Despite potential PCSE effects, children of adolescent mothers are at greater risk than children of older mothers of infant morbidity and mortality, cognitive impairment, social and behavioral deficits, child abuse and neglect, and early and pervasive school failure [44–48]. Differences between children of adolescent and adult mothers decrease, but remain significant after indices of maternal socioeconomic status are included in the analyses [49]. Moreover, the incidence of negative sequelae among these children increases with age [45, 46]. Jaffe et al. [50] reported that young adult offspring of teenage mothers were 2–3 times more likely to suffer adverse outcomes, so increased understanding of PCSE effects on these vulnerable children will identify areas where early prevention might be most effective.

The goal of this study was to examine long-term PCSE effects on the adolescent offspring of teenage mothers. To our knowledge, this is the first study to investigate PCSE effects on neurobehavioral outcomes during early adolescence in offspring of adolescent mothers. We collected trimester-specific data on maternal substance use including tobacco, alcohol, marijuana and other illicit drugs during pregnancy and in the postpartum. We assessed behavioral outcomes with multiple measures, utilizing both caregiver report and adolescent

self-report. We hypothesized that PCSE would predict an increased rate of BD problems in the adolescent offspring of adolescent mothers, and that this association would remain significant after controlling for covariates of teenage motherhood and maternal smoking.

Materials and Methods

Sample Selection and Study Design

The Teen Mother Study is part of the Maternal Health Practices and Child Development (MHPCD) project, a consortium of studies on the long-term effects of prenatal substance use. Pregnant adolescents were recruited from the Magee-Womens Hospital prenatal clinic from 1990 to 1994. Adolescents were seen during a prenatal visit and at delivery with their newborn infants. Follow-up visits were conducted with mothers and their children in our laboratory when offspring were ages 6 (1995–2000), 10 (2000–2005), and 14 years (2005–2010). The Institutional Review Boards of the Magee-Womens Hospital and the University of Pittsburgh approved each phase of this study.

The participants were recruited during the second trimester, when they came into the clinic for their fourth or fifth prenatal visit. In a private room, the pregnant adolescents were interviewed about their current and previous tobacco, alcohol, marijuana, and other drug use. The adolescents were seen again 24–36 h after delivery, when they were interviewed about their substance use during the second and third trimesters. At the 6-, 10-, and 14-year follow-up visits, the mothers provided information about their substance use (current and past year) and demographic and psychological status. Medical histories were obtained for both mothers and offspring. Reports on maternal substance use, growth of the offspring, and 6- and 10-year outcomes have been provided elsewhere [6, 10, 12]. The present study focuses on PCSE effects on BD in 14-year-old offspring (Fig. 1).

Sample Description

All adolescents attending the prenatal clinic, who were under 19 years, were eligible for the study ($n = 448$). Of those who were originally approached to participate in the study, 3 refused, for an initial refusal rate of 0.7%. Of the remaining 445 pregnant teenagers, 15 moved out of the area prior to delivery, and 1 refused the delivery interview. Additional losses included six twin births, five spontaneous abortions, two still-born infants, and three live-born premature infants who died. Thus, 413 live-born singletons and their teenage mothers were assessed at delivery. A total of 318 women and their offspring were assessed at the 14-year follow-up phase, representing 80% of the eligible birth cohort. There were 23 refusals, 54 were lost to followup, 9 had moved out of the state, 7 children had died, and 2 children were adopted. Prenatal substance exposure and SES did not differ significantly between the mothers and children who were seen and not seen at the 14-year followup.

The mothers, on average, were 16.3 years old (range = 12–18) at study recruitment: 75% were 16 years or older, and 25% were less than 15 years of age. Sixty-nine percent were African American, 31% were Caucasian, and 99% of them were unmarried at delivery [6]. At the 14-year follow-up, the mothers' average monthly income was \$2,253 (range = \$0–9,990) and their mean education was 12.8 years (range = 7–18). Most mothers (91%) had completed high school or received a GED; 3% completed college. A majority of the women (72%) were not currently married. Most of the offspring (84%) were living with their biological mothers at the age 14-year follow-up; the remaining 16% were with a custodian. If a child was not living with his or her mother, the current custodian was interviewed.

Substance Use Measures

The substance use measures used in this study were developed and extensively tested for studies of alcohol and marijuana use during pregnancy in adult women. Questions were developed to reflect accurately both the pattern and level of use [51]. At all phases of testing, the participants were interviewed in a private setting by interviewers who were comfortable discussing alcohol and drug use, trained to use the instrument reliably, accurately identify the drugs used, and assess the amount of use. For substance use during pregnancy, calendar landmarks were used to indicate time periods that corresponded with conception, recognition of pregnancy, and each trimester. To ascertain the level of cigarette smoking during pregnancy, we asked: “Do you smoke cigarettes? How old were you when you started smoking? What brand do you usually smoke? How many cigarettes do you smoke on a typical day? Has your smoking changed since you’ve been pregnant? How and when did your smoking change? How many cigarettes did you smoke on a typical day before you changed?” Average daily cigarettes was quantified using the responses of those who did not change smoking and recalculated for those who reported changes in smoking for the first trimester. At delivery, the same questions were asked covering second and third trimesters and the same procedure was used to calculate average daily cigarettes. Average daily cigarettes was the continuous measure used in our analyses. In addition, a dichotomous variable was created for each trimester to indicate any/none cigarettes per day and “10+ cigarettes per day” versus all others including those with no exposure and those with exposure of <10 cigarettes per day, to test for threshold effects. Quantity and frequency of the usual, maximum, and minimum use of each alcoholic beverage were also assessed. The average daily number of drinks was calculated from these data. Marijuana, hashish, and sinsemilla use were transformed into average daily joints: a blunt of marijuana was converted to four joints, and a hashish cigarette or bowl was counted as three joints, based on the relative amount of delta-9-THC in each [52]. Illicit drug use was rare both during pregnancy ($n = 5$) and at the 14-year follow-up phase ($n = 14$), and therefore was not considered in our analyses.

Outcome Measures

Adolescent Behavioral Dysregulation: Maternal Reports—*The Child Behavior Checklist (CBCL)* [53] has 112 problem items completed by the caretaker that provide scores for eight syndrome scales, summary internalizing and externalizing scales, and a total problem score. The problem scales include measures for anxious/depressed, withdrawn, somatic complaints, aggressive behavior, rule breaking behavior, attention problems, thought problems, and social problems. The externalizing score is made up of aggressive problems and rule breaking problems subscales. For this study, we focused on total externalization, aggression, rule breaking, attention, and social problem scores. As recommended by the manual, the age and gender adjusted t scores were used for the externalizing scale and raw scores were used for the syndrome subscales [53]. The CBCL has good test–retest reliability and discriminative validity for large normative samples. Van Dulmen and Egeland [54] examined the predictive validity of the CBCL on psychopathology at age 17.5 years and the r ’s ranged from .21 to .24 ($P < .01$) between the externalizing aggregation scores at age 7 and psychopathology at 17.5 years.

Strengths and Weaknesses of ADHD Symptoms and Normal Behavior (SWAN) [55] is a parent report of their child’s attention, impulse control and activity. The instrument is based on 18 ADHD symptoms, 9 attention deficit symptoms and 9 hyperactivity symptoms listed in DSMIV. Items are measured on a four-point scale of behavior: Not at all (0) to Very Much [3]. This scale was developed to help decrease over-diagnosis of children with ADHD [56]. Cronbach’s alphas have been reported as .97 on the inattention scale and .98 on the hyperactivity/impulsivity scale [57]. Young et al. [58] reported that all items in the SWAN

rating scale had a discrimination of between 0.77 and 0.87, meaning that these items were able to separate those children with and without ADHD.

Behavioral Dysregulation: Adolescent Self-Report

The Youth Self-Report and Profile (YSR): The YSR [59] provides a mental health profile of adolescents, similar to the CBCL, but completed by the adolescent rather than the caregiver [60]. The 112-item profile contains eight subscales, total internalizing, and total externalizing scores, and a total problem score. Our focus was on the measures best representing the construct of behavioral dysregulation including aggression, rule breaking, attention, social problems, and total externalizing behaviors. Good test–retest reliability and discriminative validity have been reported on large normative samples [60].

Revised Dimensions of Temperament Survey: The DOTS-R [61] is an assessment of dimensions of temperament consisting of nine scales. The scales of interest to this study were activity, task orientation, and distractibility. This instrument has excellent test–retest reliabilities as well as high internal consistency, and high reliability with the EAS Temperament measure used in earlier phases of the study [62].

Covariates

Based on the literature and previous findings in this cohort, measures of the offspring's environment were included in the analyses including other maternal substance use during pregnancy, maternal psychological status, demographic/family characteristics (e.g., age, ethnicity, child gender), socioeconomic status (SES), home environment, and maternal stressful life events. Maternal depressive symptoms were measured with the Center for Epidemiological Studies-Depression Scale (CES-D) [63]. The CES-D is a 20-item self-report measure developed for use in general population samples. This measure was analyzed as a continuous variable. The CES-D correlates well with other established measures of depression (e.g., Zung, $r = .90$; Beck, $r = .81$), establishing its validity [64]. The State-Trait Anxiety Inventory (STPI) [65] was used to assess dispositional (i.e., trait) anxiety and anger. Each 10-item scale was analyzed as a continuous variable. The psychometric properties of the STPI have been demonstrated in a variety of populations. The life event measure was the Psychiatric Epidemiology Research Interview Life Events Scale [66]. The Home Observation for Measurement of the Environment- Short Form (HOME-SF) [67] was used to measure the quality and quantity of support available to the adolescent for cognitive, social, and emotional development.

Data Analysis

The outcome variables were the scores on the CBCL, YSR, DOTS-R, and SWAN. First and third trimester PCSE were examined as continuous variables to test for a linear effect on the outcomes and dichotomized as any/none or as 10 or more cigarettes per day versus all others in order to test for a threshold effect. PCSE in the second trimester was highly correlated ($r = 0.96$) with third trimester PCSE, so it was not included. We excluded influential and outlier cases, identified by the modified Cook's distance [68]. A t test was used to compare the behavioral outcomes between the PCSE comparison groups without adjusting for any covariates. This was followed by a multivariate analysis. We hypothesized that PCSE was associated with increased BD and, therefore, one-sided P values were used.

PCSE effects on each of the continuous outcomes were analyzed with stepwise linear regression. Regressions were done separately for first and third trimesters and included demographic and maternal psychosocial characteristics and other prenatal substance exposures. Prenatal alcohol and marijuana exposure for first and third trimesters were dichotomized as use/no use. Measures of first trimester alcohol and marijuana exposure

were used in the first trimester analyses of PCSE, and the measure of third trimester alcohol exposure was used in third trimester analyses of PCSE. We did not control for third trimester marijuana exposure, as only 10 mothers were users in the third trimester.

Results

More than half (52%) of the pregnant teenagers used tobacco the year prior to becoming pregnant and almost half (46%) continued to smoke during the first trimester of the index pregnancy (Fig. 2). In fact, rates of smoking increased across pregnancy. However, most smokers used fewer than 10 cigarettes per day. By the third trimester, 58% of the sample used tobacco. Among the smokers, average daily quantity of smoking decreased between first and third trimesters from an average of 9 cigarettes per day to 7 cigarettes per day. These levels of cigarette smoking are lower than those reported in a similar low-SES cohort of adult-aged pregnant women who attended the same prenatal clinic [69]. Forty-eight percent of the teenagers used alcohol and 18% used marijuana in the first trimester. Alcohol and marijuana use decreased by the end of the pregnancy, with only 9% of the mothers reporting any drinking, and less than 4% continuing to use marijuana in the third trimester. Prenatal smoking was significantly associated with other prenatal substance use, so children with PCSE were also more likely to be exposed to alcohol and marijuana.

Bivariate Relations: PCSE and Covariates

Tobacco use remained high among these mothers a decade after the index delivery [70], and at the 14-year follow-up, tobacco use among the mothers remained as prevalent (51%) as the year prior to the index pregnancy (52%). The quantity of daily cigarettes smoked nearly doubled over that period: 31% smoked more than 10 cigarettes per day as compared to 18% who smoked at this level before pregnancy (Fig. 2). There were demographic differences between the mothers who smoked and those who had not smoked during pregnancy. The mothers who smoked in the first trimester were more likely to be married or to have a man in the household ($P < .05$). Caucasian mothers were more likely to smoke cigarettes (69.6% vs. 36.3% African American mothers; $P < .001$) and smoke at heavier levels (8.5 cigs/day vs. 2.5 cigs/day; $P < .001$). Those who smoked during pregnancy reported higher symptoms of depression ($P < .05$) and hostility ($P < .05$) and more life events ($P < .05$) at the 14-year follow-up. However, there were no statistically significant differences between prenatal smokers and nonsmokers in family income or quality of the home environment at 14 years postpartum.

Bivariate Relations: PCSE and BD Outcomes

There were significant bivariate associations between PCSE and BD outcomes at age 14. Most of the associations were with first trimester PCSE (Table 1), comparing exposure at 10+ cigarettes per day to no exposure. Adolescents with first trimester PCSE of 10 or more daily cigarettes had higher externalizing problems ($P < .001$), aggression ($P < .001$), rule breaking ($P < .001$), social ($P = .010$), and attentional problem scores ($P = .015$) on the CBCL and on the YSR ($P = .046$; $P = .044$; $P = .016$; $P = .005$, respectively) (with the exception of rule breaking problems, which did not reach significance on the YSR). PCSE at 10+ cigarettes was also related to greater inattention and hyperactivity as measured by the SWAN, and more problems with distractibility and task orientation as measured by the DOTS-R. Fewer of the BD outcomes were related to third trimester PCSE, and significance levels were less robust. The only significant relations between third trimester PCSE and BD outcomes included CBCL total externalizing ($P = .020$), rule breaking problems ($P = .027$), social problems ($P = .042$), YSR attention problems ($P = .044$) and DOTS-R distractibility ($P = .050$) when the group of exposure of 10+ cigarettes per day was compared to no

exposure. When comparing 10+ cigarettes per day to <10 cigarettes per day, only DOTS-R distractibility was significantly related to exposure (Table 2).

Multivariate Relations: PCSE and BD Outcomes

Covariates for all multivariate analyses included demographic characteristics, prenatal exposure to other substances, and maternal psychological characteristics (Table 3). First or third trimester PCSE was included separately in each model and was considered separately as: (1) continuous (average daily cigarettes); (2) dichotomous variable (10 or more cigarettes per day); (3) dichotomous variable (any/none).

First Trimester PCSE—After adjusting for covariates, offspring with first trimester PCSE exposure had significantly more BD on both the maternal (CBCL) and self-- reports (YSR). These included: total externalizing behaviors (CBCL), aggression (CBCL, YSR), rule breaking problems (CBCL), and social problems (CBCL). Most associations with BD were found with 10+ cigs/day; however, average daily quantity of cigarettes was also related to greater total externalizing and rule breaking problems. Among the SWAN outcomes, any PCSE predicted greater activity and PCSE (any/none, 10+ cigs/day, and average daily quantity) predicted more problems with inattention. Similarly, all three PCSE variables predicted more distractibility (DOTS-R).

Third Trimester PCSE—After adjusting for covariates, third trimester PCSE (10+ cigs/day, any, and average quantity) predicted more total externalizing problems (CBCL) and more social problems on both the CBCL and YSR (10+ cigs/day, any). PCSE also predicted inattention (SWAN) and distractibility (DOTS-R) (Table 4).

Other significant covariates of the BD outcomes included maternal psychological status such as maternal anxiety, hostility, and depression, depending on the outcome. A poorer home environment and more maternal life events were environmental factors that contributed to several of the BD outcomes. Demographic factors including lower income, maternal education, offspring gender (male), race (African-American), and age (younger) were also significant predictors of certain BD outcomes. Prenatal alcohol exposure from the third trimester (any) significantly predicted more problems with inattention. We also examined the potential interaction between race and PCSE effects. This interaction was significant for only one outcome, CBCL social problems. For this outcome variable, PCSE was a significant predictor for increased social problems among African Americans, but not among Caucasians.

Discussion

In this study, offspring with PCSE had more social problems, aggressive and rule breaking behaviors, and total externalizing behaviors than non-exposed offspring. They were more active, inattentive, easily distracted and had more problems with task orientation. These results were generally first trimester effects, and were seen mostly when PCSE was dichotomized at 10 or more cigarettes/day. In the animal literature, fetal nicotine exposure results in altered physiology at neuronal sites that control arousal and more excitability [71]. Nicotine-induced inhibition of the monamine oxidase system during fetal development has been implicated in the relation between smoking during pregnancy and offspring aggression [30]. This literature also provides further biological support for our findings of prenatal nicotine exposure and increased motor activity [41, 72–74] related to an increase in cortical nicotinic receptors [75]. This increase in activity is comparable to the increased activity and associated behavior problems seen in exposed human offspring. Demographic predictors of

externalizing behavior included male sex and African- American race, which are consistent findings with reports in the human literature [21, 76, 77].

This is the first study of PCSE effects on behavior dysregulation in the offspring of adolescent mothers. It is particularly noteworthy that PCSE effects were still measurable 14 years post-partum. Since levels of smoking are generally lower among pregnant teenagers as compared to adults [7, 18], this means that exposure on the offspring is also lower than that usually found among offspring of pregnant adults. Most of the PCSE effects resulted from exposure during the first trimester and from a threshold of 10 or more cigarettes/day. This suggests that at lower levels of PCSE, there may be no effect, or the effect may not be detectable with these measures. Many of our significant results were from both the caregiver and self reports. We controlled for variables such as maternal hostility and depression that were also independently related to the outcome, underscoring the importance of considering of these factors in future research on PCSE effects on offspring. However, it should be noted that the amount of variance in behavior problems explained by PCSE, while significant was small. We included a large number of environmental and psychosocial predictors of behavioral dysregulation in our model and each factor predicted only a small portion of the explained variance in behavioral dysregulation. Thus, although there is a statistically significant relation between PCSE and BD, this relationship explains a small portion of the overall variability in BD.

This study has multiple strengths. The women were pregnant adolescents who attended a prenatal clinic and their tobacco, alcohol, and other drug use represented the entire spectrum of adolescent drug behavior from abstention to heavy use. In addition, other prenatal substance exposures were measured prospectively and controlled in the statistical analyses. Third trimester prenatal alcohol exposure predicted attentional deficits in our analyses, which is consistent with other studies [78, 79]. We did not find any relation between prenatal marijuana exposure and offspring and BD in offspring, contrary to other reports [80, 81]. However, marijuana use was very low in our sample. This study also decreased possible bias from mothers' psychological status by adjusting her psychological measures in the analysis.

This study also had limitations. Our sample represented pregnant teenagers who attended a large inner-city hospital prenatal clinic. Although this is not a general population sample, it does represent the majority of births to teenaged women in the city of Pittsburgh. The racial distribution of our sample is also representative of a population of pregnant teenagers who attend an inner city prenatal clinic, with 70% being Black. We found that black pregnant teenagers were less likely to smoke and to smoke at lower levels than white pregnant teenagers. However, there is evidence that blacks may have higher cotinine levels than whites even when smoking the same number of cigarettes between both non pregnant [82] and pregnant adults [83]. This difference is thought to be due, in part, to a slower metabolism of nicotine in Blacks [84]. However, we did not have biological measures which provided cotinine levels, and PCSE exposure was based on maternal self-report rather than biological measures. Biological measures have disadvantages, measuring use for only a short window of time, whereas questionnaire data can elicit patterns of use over time. As tobacco and other drug use tend to be more sporadic among teenagers than adults [7], biological measures may miss a significant amount of use. To increase the accuracy of the reported data, we constructed detailed questions, thoroughly tested our measures, carefully selected interviewers, and extensively trained our staff in interview techniques. The correlations between reports from each trimester of pregnancy were high demonstrating consistency in reporting, an indication that maternal reports were accurate. Longitudinal cohort analyses can also be strengthened with genetic data [85]. Although our study did not collect genetic material, we did control for maternal psychological symptoms, including

depression and hostility, to account for the shared genetic liability for cigarette use and behavioral dysregulation in both the mother and offspring. Finally, we collected measures of environmental smoke when the offspring were age 6, but did not collect this information at age 14 when they could be active users. ETS is also independently related to behavioral outcomes [86], and we were not able account for this potential effect when the offspring were age 14 years. However, when the offspring of this cohort were examined at age 6, ETS was not a significant predictor of child behavior whenever PCSE was included in the model [12].

Conclusions

Our findings on PCSE and offspring behavior are consistent with earlier results, when the children were assessed at 6 and 10 years of age [10, 11], and expand the findings to those behaviors that comprise the dysregulation construct. At earlier ages, we found that PCSE predicted increased activity levels and more attention problems as well as more total externalizing behaviors, and problems with selective attention and response inhibition. Our findings are strengthened in this study when we utilized both maternal reports of behaviors as well as the adolescent's self-evaluation. This consistency of findings over time gives credence to our results and adds to the converging evidence that PCSE offspring will continue to have behavior problems as they mature and these problems may affect later adolescent and young adult functioning. Moffitt [87] described a pattern of life-course persistent antisocial and disruptive behaviors where problems with attention and aggression that surface in early development can persist as delinquent behavior in adolescence and even criminal behavior in adulthood. Identifying exposed offspring early in life with effective intervention strategies can potentially break this pathway over time and ultimately prevent more serious adolescent and adult PCSE-related behaviors.

References

1. Darroch, J.; Frost, J.; Singh, S. Occasional report. New York: AGI; 2001. Teenage sexual and reproductive behavior in developed countries: Can more progress be made?; p. 14
2. Allen A, Dietz P, Tong V, et al. Prenatal smoking prevalence ascertained from two population-based data sources: Birth certificates and PRAMS questionnaires, 2004. Public Health Reports. 2008; 123:586–592. [PubMed: 18828413]
3. Johnston, L.; O'Malley, P.; Bachman, J., et al. NIH Publication No. 05-5726. Bethesda, MD: National Institute on Drug Abuse; 2005. Monitoring the future national results on adolescent drug use: Overview of key findings, 2004.
4. Hamilton, B.; Martin, J.; Ventura, S. National vital statistics reports. 2007. Births: Preliminary data for 2006; p. 56
5. Batstra L, Hadders-Algra M, Neeleman J. Effect of antenatal exposure to maternal smoking on behavioural problems and academic achievement in childhood: Prospective evidence from a Dutch birth cohort. Early Human Development. 2003; 75:21–33. [PubMed: 14652157]
6. Cornelius M, Taylor P, Geva D. Prenatal tobacco and marijuana use among adolescents: Effects on offspring gestational age, growth and morphology. Pediatrics. 1995; 95:438–443.
7. Cornelius, M.; Day, N.; Richardson, R., et al. Epidemiology of substance abuse during pregnancy. In: Ott, P.; Tarter, R.; Ammerman, R., editors. Sourcebook on substance abuse: Etiology, epidemiology, assessment and treatment. Needham Heights, MA: Allyn and Bacon; 1999. p. 1-13.
8. Cornelius M, Day N. Effects of prenatal and postnatal tobacco exposures on offspring: A review. Alcohol Health and Research World. 2000; 24:242–249.
9. Cornelius M, Goldschmidt L, Day N, et al. Alcohol, tobacco, and marijuana use among pregnant teenagers: Six-year follow-up of offspring growth effects. Neurotoxicology and Teratology. 2002; 24:703–710. [PubMed: 12460652]

10. Cornelius M, Goldschmidt L, De Genna N. Smoking during teenage pregnancies: Effects on behavioral problems in offspring. *Nicotine and Tobacco Research*. 2007; 9:739–750. [PubMed: 17577803]
11. Cornelius M, Day N. Developmental consequences of prenatal tobacco exposure. *Current Opinion in Neurology*. 2009; 22:121–125. [PubMed: 19532034]
12. Cornelius M, De Genna N, Leech S, Willford J. Effects of prenatal tobacco exposure on neurobehavioral outcomes of 10-year-old children of teenage mothers. *Neurotoxicology and Teratology*. 2011; 33:137–144. [PubMed: 21256428]
13. Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. *Environmental Health Perspectives*. 1999; 107:991–1000. [PubMed: 10585903]
14. Huizink A, Mulder E. Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring. *Neuroscience and Biobehavioral Reviews*. 2006; 20:24–41. [PubMed: 16095697]
15. Mansi G, Raimondi F, Pichini S. Neonatal urinary cotinine correlates with behavioral alterations in newborns prenatally exposed to tobacco smoke. *Pediatric Research*. 2007; 61:257–261. [PubMed: 17237732]
16. Martin L, McNamara M, Milot A, et al. Correlates of smoking before, during, and after pregnancy. *American Journal of Health Behavior*. 2008; 32:272–282. [PubMed: 18067467]
17. Stroud L, Paster R, Goodwin M. Maternal smoking during pregnancy and neonatal behavior: A large-scale community study. *Pediatrics*. 2009; 123:e842–e848. [PubMed: 19403478]
18. Willford, J.; Day, N.; Cornelius, M. Maternal tobacco use during pregnancy: Epidemiology and effects on offspring. In: Miller, M., editor. *Development of the mammalian central nervous system: Lessons learned from studies on alcohol and nicotine exposure*. New York: Oxford University Press; 2006. p. 315–328.
19. Kotimaa A, Moilanen I, Taanila A, et al. Maternal smoking and hyperactivity in 8-year-old children. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42:826–833. [PubMed: 12819442]
20. Langley K, Turic D, Rice F, et al. Testing for gene X environment interaction effects in attention deficit hyperactivity disorder and associated antisocial behavior. *American Journal of Medical Genetics, Part B (Neuropsychiatric genetics)*. 2008; 147B:49–53.
21. Linnet K, Dalsgaard S, Obel C. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: Review of current evidence. *American Journal of Psychiatry*. 2003; 160:1028–1040. [PubMed: 12777257]
22. Mick E, Biederman J, Faraone S, Sayor J, et al. Case-control study of attention-deficit hyperactivity disorder and maternal smoking, alcohol use, and drug use during pregnancy. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:378–385. [PubMed: 11931593]
23. Milberger S, Biederman S, Faraone S, et al. Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? *American Journal of Psychiatry*. 1996; 153:1138–1142. [PubMed: 8780415]
24. Thapar A, Fowler T, Rice F, et al. Maternal smoking during pregnancy and attention deficit hyperactivity disorder symptoms in offspring. *American Journal of Psychiatry*. 2003; 160:1985–1989. [PubMed: 14594745]
25. Button T, Thapar A, McGuffin P. Relationship between antisocial behaviour, attention-deficit hyperactivity disorder and maternal prenatal smoking. *British Journal of Psychiatry*. 2005; 187:155–160. [PubMed: 16055827]
26. Carter S, Paterson J, Gao W. Maternal smoking during pregnancy and behaviour problems in a birth cohort of 2-year-old Pacific children in New Zealand. *Early Human Development*. 2008; 84:59–66. [PubMed: 17499944]
27. Day N, Richardson G, Goldschmidt L, et al. Effects of prenatal tobacco exposure on preschooler's behavior. *Journal of Developmental and Behavioral Pediatrics*. 2000; 21:180–188. [PubMed: 10883878]

28. Gatzke-Kopp L, Beauchaine T. Direct and passive prenatal nicotine exposure and the development of externalizing psychopathology. *Child Psychiatry and Human Development*. 2007; 38:255–269. [PubMed: 17520361]
29. Robinson M, Oddy W, Li J, et al. Pre- and postnatal influences on preschool mental health: A large-scale cohort study. *Journal of Child Psychology and Psychiatry Allied Disciplines*. 2008; 49:1118–1128.
30. Baler R, Volkow N, Fowler J, Benveniste H. Is fetal brain monoamine oxidase inhibition the missing link between maternal smoking and conduct disorders? *Journal of Psychiatry & Neuroscience*. 2008; 33:187–195. [PubMed: 18592036]
31. Fergusson D, Horwood L, Ridder E. Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence. *Drug And Alcohol Dependence*. 2007; 88S:S14–S26. [PubMed: 17292565]
32. Maughan B, Taylor A, Caspi A, et al. Prenatal smoking and early childhood conduct problems: Testing genetic and environmental explanations of the association. *Archives of General Psychiatry*. 2004; 61:836–843. [PubMed: 15289282]
33. Ruckinger S, Rzehak P, Chen C, et al. Prenatal and postnatal tobacco exposure and behavioral problems in 10-year old children: Results from the GINI-plus study group. *Environmental Health Perspectives*. 2010; 118:150–154. [PubMed: 20056582]
34. Wakschlag L, Leventhal B, Pine D, Pickett K, Carter A. Elucidating early mechanisms of developmental psychopathology: The case of prenatal smoking and disruptive behavior. *Child Development*. 2006; 77:893–906. [PubMed: 16942496]
35. Wakschlag L, Pickett K, Cook E, et al. Maternal smoking during pregnancy and severe antisocial behavior in offspring: A review. *American Journal of Public Health*. 2002; 92:966–974. [PubMed: 12036791]
36. Pickett K, Rathouz P, Dukic V, et al. The complex enterprise of modeling prenatal exposure to cigarettes: What is enough? *Paediatric and Perinatal Epidemiology*. 2009; 23:160–170. [PubMed: 19159402]
37. Brion M, Victora C, Matjasevich A, et al. Maternal smoking and child psychological problems: Disentangling causal and noncausal effects. *Pediatrics*. 2010; 126:e57–e65. [PubMed: 20587678]
38. Huijbregts S, Séguin J, Zoccolillo M, et al. Maternal prenatal smoking, parental antisocial behavior, and early childhood physical aggression. *Development and Psychopathology*. 2008; 20:437–453. [PubMed: 18423088]
39. Ernst M, Moolchan E, Robinson M. Behavioral and neural consequences of prenatal exposure to nicotine. *Journal of the American Academy of Child Adolescent Psychiatry*. 2001; 40:630–642.
40. Tarter R, Kirisci L, Mezzich A, et al. Neurobehavioral disinhibition in early childhood predicts early age onset of substance use disorder. *American Journal of Psychiatry*. 2003; 160:1078–1085. [PubMed: 12777265]
41. Slotkin T. If nicotine is a developmental neurotoxicant in animal studies, dare we recommend nicotine replacement therapy in pregnant women and adolescents? *Neurotoxicology and Teratology*. 2008; 30:1–19. [PubMed: 18380035]
42. Adams K, Melvin C, Raskind-Hood C. Sociodemographic, insurance, and risk profiles of maternal smokers post the 1990s: How can we reach them? *Nicotine and Tobacco Research*. 2008; 10:1121–1129. [PubMed: 18629721]
43. Burns L, Mattick R, Wallace C. Smoking patterns and outcomes in a population of pregnant women with other substance use disorders. *Nicotine and Tobacco Research*. 2008; 10:969–974. [PubMed: 18584460]
44. Babsin S, Clark M. Relationships between infant death and maternal age. *Journal of Pediatrics*. 1983; 103:391–393. [PubMed: 6886903]
45. Furstenberg F, Levine J, Brooks-Gunn J. The children of teenage mothers: Patterns of early childbearing in two generations. *Family Planning Perspectives*. 1990; 22:54–61. [PubMed: 2347409]
46. Moore K, Snyder N. Cognitive attainment among firstborn children of adolescent mothers. *American Sociological Review*. 1991; 56:612–624.

47. Sommer K, Whitman T, Borkowski J, et al. Prenatal maternal predictors of cognitive and emotional delays in children of adolescent mothers. *Adolescence*. 2000; 35:87–112. [PubMed: 10841299]
48. Zuckerman B, Walker D, Frank DA. Adolescent pregnancy and biobehavioral determinants of outcome. *Journal of Pediatrics*. 1984; 105:857–863. [PubMed: 6389811]
49. Children's Defense Fund. Clearinghouse paper no 1. Washington, DC: Children's Defense Fund; 1985. Preventing children having children.
50. Jaffe S, Caspi A, Moffitt T, et al. Why are children born to teen mothers at risk for adverse outcomes in young adulthood? Results from a 20-year longitudinal study. *Development and Psychopathology*. 2001; 12:377–397.
51. Day N, Robles N. Methodological issues in the measurement of substance use. *Annals of the New York Academy of Sciences*. 1989; 562:8–13. [PubMed: 2742287]
52. Gold, M. Marijuana. New York: Plenum; 1989.
53. Achenbach, T.; Rescorla, L. Manual for the ASEBA school-age forms & profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families; 2001.
54. Van Dulmen M, Egeland B. Analyzing multiple informant data on child and adolescent behavior problems: Predictive validity and comparison of aggregation procedures. *International Journal of Behavioral Development*. 2011; 35:84–92.
55. Swanson, J.; Schuck, S.; Mann, M.; Carlson, C.; Hartman, K.; Sergeant, J. The SWAN rating scale. Available at <http://www.adhd.net>
56. Swanson, J.; Schuck, S.; Mann, M.; Carlson, C.; Hartman, K.; Sergeant, J.; Clevenger, W., et al. Categorical and dimensional definitions and evaluations of symptoms of ADHD: The SNAP and the SWAN rating scales. 2001. http://www.adhd.net/SNAP_SWAN.pdf
57. Foley M, McClowry S, Castellanos F. The relationship between attention deficit hyperactivity disorder and child temperament. *Journal of Applied Developmental Psychology*. 2008; 29:157–169.
58. Young D, Levy F, Martin N, Hay D. Attention deficit hyperactivity disorder: A rasch analysis of the SWAN rating scale. *Child Psychiatry and Human Development*. 2009; 40:543–559. [PubMed: 19455417]
59. Achenbach, T. Manual for the youth self-report and 1991 profile. Burlington, VT: University of Vermont, Department of Psychiatry; 1991.
60. McConaughy S, Achenbach T, Gent C. Multiaxial empirically based assessment: Parent, teacher, observational, cognitive, and personality correlates of child behavior profiles for 6–11 year-old boys. *Journal of Abnormal Child Psychology*. 1988; 16:485–509. [PubMed: 3235743]
61. Windle M, Lerner R. Reassessing the dimension of temperamental individuality across the life span: The revised dimensions of temperament survey (DOTS-R). *Journal of Adolescent Research*. 1986; 1:213–230.
62. Windle M. Temperament and personality: An exploratory interinventory study of the DOTS-R, EASI-II, and EPI. *Journal of Personality Assessment*. 1989; 53:487–501.
63. Radloff L. The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1:385–401.
64. Myers J, Weissman M. Use of a self-report symptom scale to detect depression in a community sample. *American Journal of Psychiatry*. 1980; 137:1081–1084. [PubMed: 7425160]
65. Spielberger, C.; Gorsuch, R.; Lushene, R. Manual for the state trait anxiety inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
66. Dohrenwend, B.; Dohrenwend, B. Stressful life events: Their nature and effects. Wiley; New York: 1974.
67. Baker, P.; Mott, F. National longitudinal study of youth child handbook. Columbus, OH: Center for Human Resources Research, Ohio State University; 1989.
68. Cook, R.; Weisberg, S. Residuals and influence in regression. New York: Chapman and Hall; 1982.

69. Day N, Cornelius M, Goldschmidt L, et al. The effects of prenatal tobacco and marijuana use on offspring growth from birth through age 3 years. *Neurotoxicology and Teratology*. 1992; 14:407–414. [PubMed: 1488035]
70. DeGenna N, Donovan J, Cornelius M. Tobacco and marijuana use before teenage pregnancy and ten years later. *Addictive Behaviors*. 2009; 34:463–470. [PubMed: 19179015]
71. Good C, Bay K, Buchanan R, et al. Prenatal exposure to cigarette smoke affects the physiology of pedunculopontine nucleus (PPN) neurons in development. *Neurotoxicology and Teratology*. 2006; 28:210–219. [PubMed: 16469482]
72. Pauly J, Sparks J, Hauser K, et al. In utero nicotine exposure causes persistent, gender-dependant changes in locomotor activity and sensitivity to nicotine in C57B1/6 mice. *International Journal of Developmental Neuroscience*. 2004; 22:329–337. [PubMed: 15380832]
73. Thomas J, Garrison M, Slaweki C, et al. Nicotine exposure during the neonatal brain growth spurt produces hyperactivity in preweanling rats. *Neurotoxicology and Teratology*. 2000; 22:695–701. [PubMed: 11106862]
74. Tizabi Y, Popke E, Rahman M, et al. Hyperactivity induced by prenatal nicotine exposure is associated with an increase in cortical nicotinic receptors. *Pharmacology, Biochemistry and Behavior*. 1997; 58:141–146.
75. Vaglenova J, Birru S, Pandiella N, et al. An assessment of the long-term developmental and behavioral teratogenicity of prenatal nicotine exposure. *Behavioural Brain Research*. 2004; 150:159–170. [PubMed: 15033289]
76. McLaughlin K, Hilt L, Nolen-Hoeksema S. Racial/ethnic differences in internalizing and externalizing symptoms in adolescents. *Journal of Abnormal Child Psychology*. 2007; 35:801–816. [PubMed: 17508278]
77. Moffitt, T.; Caspi, A.; Rutter, M., et al. Sex differences in antisocial behavior: Conduct disorder, delinquency, and violence in the Dunedin longitudinal study. Cambridge, UK: Cambridge University Press; 2001.
78. Coles C, Platzman P, Raskind-Hood C. A comparison of children affected by prenatal alcohol exposure and attention deficit hyperactivity disorder. *Alcoholism: Clinical and Experimental Research*. 1997; 20:150–161.
79. Jacobson J, Jacobson S. Effects of prenatal alcohol exposure on child development. *Alcohol Research & Health*. 2002; 26:282–286. [PubMed: 12875038]
80. Fried P. Adolescents prenatally exposed to marijuana: Examination of facets of complex behavior and comparison with the influence of in utero cigarettes. *Journal of Clinical Pharmacology*. 2002; 42:97S–102S. [PubMed: 12412842]
81. Goldschmidt L, Day N, Richardson G. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicology and Teratology*. 2000; 22:325–336. [PubMed: 10840176]
82. Caraballa R, Giovino G, Pechacek T, Mowery P, Strauss W, Sharp D, et al. Racial and ethnic differences in serum cotinine levels of cigarettes smokers: Third national health and nutrition examination survey, 1988–1991. *JAMA*. 1998; 280:135–139. [PubMed: 9669785]
83. English P, Eskenazi B, Christianson R. Black-white differences in serum cotinine levels among pregnant women and subsequent effects on infant birthweight. *American Journal of Public Health*. 1994; 84:1439–1443. [PubMed: 8092368]
84. Perez-Stable E, Herrera B, Jacob P, Benowitz N. Nicotine metabolism and intake in black and white smokers. *JAMA*. 1998; 280:152–156. [PubMed: 9669788]
85. Golding G. The importance of a genetic component in longitudinal birth cohorts. *Paediatric and Perinatal Epidemiology*. 2009; 23:174–184. [PubMed: 19490455]
86. Yolton K, Khoury J, Hornung R, Dietrich K, Succop P, Lanphear B. Environmental tobacco smoke exposure and child behaviors. *Journal of Developmental and Behavioral Pediatrics*. 2008; 29:450–457. [PubMed: 19093323]
87. Moffitt T. Adolescent-limited and life-course-persistent antisocial behavior: A developmental taxonomy. *Psychological Reviews*. 1993; 100:674–701.

Fig. 1.
Study design

Fig. 2.
Prevalence of maternal smoking from pre-pregnancy to 14 years postpartum. (None = 0 cigs/day; Light = 0–9 cigs/day; Moderate = 10–19 cigs/day; Heavy = 20+ cigs/day)

Table 1

Unadjusted analyses: mean scores on behavior dysregulation outcomes by first trimester PCSE

BD measure	Scale	NO PCSE group 1	PCSE 1 to < 10 cig/day group 2	PCSE 10+ cig/day group 3	P value 3 vs. 1	P value 3 vs. 1 and 2
CBCL	Total externalizing	51.1	51.4	55.9	< 0.001	< 0.001
	Aggression	4.9	4.4	7.2	0.002	< 0.001
	Rule breaking	2.9	2.9	4.4	0.001	< 0.001
	Social problems	1.6	1.5	2.3	0.015	0.010
	Attention problems	3.3	3.6	4.6	0.013	0.015
YSR	Total externalizing	51.1	51.6	53.9	0.046	0.049
	Aggression	6.7	6.9	8.1	0.044	0.045
	Rule breaking	4.1	4.0	4.7	0.113 NS	0.086 NS
	Social problems	2.6	3.1	3.5	0.016	0.038
SWAN	Attention problems	5.0	5.3	6.4	0.005	0.007
	Inattention	3.0	3.8	4.5	< 0.001	< 0.001
	Hyperactivity	1.6	2.2	2.6	0.006	0.015
	Distractibility [#]	12.0	11.6	10.9	0.007	0.013
DOTS-R	Task orientation	20.2	19.6	18.7	0.013	0.070 NS
	Activity	17.7	18.0	18.2	0.278 NS	0.375 NS

[#] Lower scores indicate higher distractibility

Table 2

Unadjusted analyses: mean scores on behavior dysregulation outcomes by third trimester PCSE

BD measure	Scale	NO PCSE group 1	PCSE 1 to < 10 cig/day Group 2	PCSE 10+ cig/day Group 3	P value 3 vs. 1	P value 3 vs. 1 and 2
CBCL	Total externalizing	50.5	53.0	53.8	0.020	0.080 NS
	Aggression	4.8	5.4	5.9	0.086 NS	0.139 NS
	Rule breaking	2.7	3.5	3.7	0.027	0.091 NS
	Social problems	1.4	1.8	2.0	0.042	0.080 NS
	Attention problems	3.3	3.8	3.9	0.150 NS	0.056 NS
YSR	Total externalizing	50.7	52.2	52.8	0.118 NS	0.200 NS
	Aggression	6.5	7.2	7.6	0.083 NS	0.152 NS
	Rule breaking	4.0	4.2	4.5	0.178 NS	0.208 NS
	Social problems	2.5	3.3	3.0	0.110 NS	0.343 NS
	Attention problems	5.1	5.3	6.0	0.044	0.056 NS
SWAN	Inattention	3.0	3.9	3.6	0.075 NS	0.300 NS
	Hyperactivity	1.8	2.1	2.0	0.279 NS	0.415 NS
	Distractibility [#]	11.9	11.8	11.1	0.044	0.050
DOTS-R	Task orientation	20.0	19.9	18.9	0.074 NS	0.064 NS
	Activity	17.9	17.6	18.3	0.295 NS	0.209 NS

[#] Lower scores indicate higher distractibility

Table 3

Adjusted analyses: first trimester PCSE and other significant predictors of behavior dysregulation outcomes

BD measure	Scale	PCSE (β = Beta values, t = t tests)	Significant covariates (β = Beta values, t = t tests)	R ²
CBCL	Total externalizing	1st trimester ^b	Income (β = -0.15, t = -4.16) ***	.16
		10+ cigs/day (β = 4.92, t = 3.64) ***	Maternal education (β = 0.69, 1.78) *	
		1st trimester	Maternal anxiety (β = 0.29, t = 2.35) **	
		Average cigs/day (β = 0.23, 2.84) **	Maternal hostility (β = 0.27, t = 1.86) *	
	Aggression problems	1st trimester ^b	Income (β = -0.07, t = -3.80) ***	.17
		10 + cigs/day (β = 2.45, t = 3.63) ***	Maternal education (β = 0.36, t = 1.87) *	
			Income (β = -0.68, t = 2.0) *	
			Maternal anxiety (β = 0.14, t = 4.24) ***	
	Rule breaking problems	1st trimester ^b	African American ethnicity (β = 0.90, t = 2.15) *	.14
		10 + cigs/day (β = 1.80, t = 3.79) ***	Male child (β = -0.90, t = 3.62) ***	
		1st trimester	Child age (β = 0.61, t = 2.11) *	
		Average cigs/day (β = 0.06, t = 2.10) *	Income (β = -0.02, t = -2.32) *	
	Social problems	1st trimester ^b	Maternal anxiety (β = 0.14, t = 5.56) ***	.13
			African American ethnicity (β = 0.77, t = 2.66) **	
		10 + cigs/day (β = 1.07, t = 3.21) ***	Child age (β = -0.35, t = -1.73) *	
			Maternal anxiety (β = 0.10, t = 4.46) ***	
YSR	Aggression problems	1st trimester ^b	Life events (β = 0.08, t = 1.85) *	.04
		10 + cigs/day (β = 1.36, t = 1.71)	Male child (β = -1.38, t = -2.31) *	
SWAN	Hyperactivity	1st trimester ^b	Maternal hostility (β = 0.11, t = 1.75) *	.18
		Any/none (β = 0.60, 2.05)	Maternal hostility (β = 0.11, t = 1.75) *	
			Income (β = -0.02, -2.48) *	
			Maternal anxiety (β = 0.09, 3.30) ***	
	Inattention	1st trimester ^b	Male child (β = 0.65, t = 2.27) *	.17
		10 + cigs/day (β = 1.21, t = 3.32)	Income (β = -0.03, -3.48) ***	
		1st trimester	Maternal anxiety (β = 0.12, t = 4.44) ***	
		Average cigs/day (β = 0.05, t = 2.47)		
DOTS-R	Distractibility ^a	1st trimester		.03
		Any/None cigs/day (β = 0.96, t = 3.36)		
		1st trimester ^b	Home environment (β = 0.11, t = 1.70) *	
		10 + cigs/day (β = -1.00, t = -2.26)		
		1st trimester		
		Average cigs/day (β = -0.06, t = -2.18)		
		1st trimester		
		Any/none cigs/day (β = -0.73, t = -2.15)		

^a Lower scores indicate more distractibility

^b Significant covariates are reported with the identified PCSE exposure variable

*
 $P < 0.05$,

**
 $P < 0.01$,

 $P < 0.001$

Table 4

Adjusted analyses: third trimester PCSE and other significant predictors of behavior dysregulation outcomes

BD measure	Scale	PCSE (β = Beta values, t = t tests)	Significant covariates (β = Beta values, t = t tests)	R ²
CBCL	Total externalizing	3rd trimester ^b	Income (β = -0.12, t = -3.71) ***	.12
		10+ cigs/day (β = 2.59, t = 1.87) *	Maternal anxiety (β = 0.43, t = 4.33) ***	
		3rd trimester		
		Average cigs/day (β = 0.15, t = 1.72) *		
		3rd trimester		
		Any/none cigs/day (β = 1.93, t = 1.76) *		
	Social problems	3rd trimester *	African American ethnicity (β = 0.68, t = 2.38) **	.13
		10+ cigs/day (β = 0.88, t = 2.64) **	Child age (β = -0.33, t = -1.65) *	
			Maternal anxiety (β = 0.10, t = 4.48) ***	
			Life events (β = 0.10, t = 2.25) ***	
YSR	Social problems	3rd trimester ^b	None	.03
		Any/none cigs/day (β = 0.66, t = 2.10) **		
SWAN	Inattention	3rd trimester ^b	3rd trimester alcohol exposure (yes/no) (β = 1.54, t = 2.73) **	.18
		Average cigs/day (β = 0.04, t = 1.72) *		
		3rd trimester	Male sex (β = 0.73, t = 2.52) **	
		Any/None cigs/day (β = 0.49, t = 1.67) *	Income (β = -0.02, t = -2.51) **	
	Distractibility ^a		Maternal anxiety (β = 0.11, t = 4.13) ***	.02
			Home environment (β = -0.11, t = -1.82) *	
		3rd trimester ^b	Home Environment (β = 0.11, t = 1.71) *	
		Average cigs/day (β = -0.06, t = -2.00) *		

^aLower scores indicate more distractibility^bSignificant covariates are reported with the identified PCSE exposure variable* $P < 0.05$,** $P < 0.01$,*** $P < 0.001$