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Preadolescent behavior problems after prenatal cocaine exposure: Relationship between teacher and caretaker ratings (Maternal Lifestyle Study)

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Abstract

Background—We previously reported an association between prenatal cocaine exposure (PCE) and childhood behavior problems as observed by the parent or caretaker. However, these behavior problems may not manifest in a structured environment, such as a school setting.

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Objective—We determined whether there is an association between PCE and school behavior problems and whether ratings of behavior problems from the teacher differ from those noted by the parent or caretaker.

Methods—The Maternal Lifestyle Study, a multicenter study, enrolled 1388 children with and without PCE at one month of age for longitudinal assessment. Teachers masked to prenatal drug exposure status completed the Teacher Report Form (TRF/6-18) when children were 7, 9, and 11 years old. We also administered the Child Behavior Checklist-parent report (CBCL) to the parent/caretaker at same ages and then at 13 years. We performed latent growth curve modeling to determine whether high PCE will predict externalizing, internalizing, total behavior, and attention problems at 7 years of age and whether changes in problems' scores over time differ between those exposed and non-exposed from both teacher and parent report. Besides levels of PCE as predictors, we controlled for the following covariates, namely: site, child characteristics (gender and other prenatal drug exposures), family level influences (maternal age, depression and psychological symptomatology, continuing drug use, exposure to domestic violence, home environment, and socioeconomic status), and community level factors (neighborhood and community violence).

Results—The mean behavior problem T scores from the teacher report were significantly higher than ratings by the parent or caretaker. Latent growth curve modeling revealed a significant relationship between intercepts of problem T scores from teacher and parent ratings; i.e., children that were rated poorly by teachers were also rated poorly by their parent/caretaker or vice versa. After controlling for covariates, we found high PCE to be a significant predictor of with higher externalizing behavior problem T scores from both parent and teacher report at 7 years ($p=0.034$ and $p=0.021$, respectively) in comparison to non-PCE children. These differences in scores from either teacher or caregiver were stable through subsequent years or did not change significantly over time. Boys had higher T scores than girls on internalizing and total problems by caretaker report; they also had significantly higher T scores for internalizing, total, and attention problems by teacher ratings; the difference was marginally significant for externalizing behavior ($p=0.070$). Caretaker postnatal use of tobacco, depression, and community violence were significant predictors of all behavior problems rated by parent/caretaker, while lower scores on the home environment predicted all behavior outcomes by the teacher report.

Conclusions—Children with high PCE are likely to manifest externalizing behavior problems; their behavior problem scores at 7 years from either report of teacher or parent remained higher than scores of non-exposed children on subsequent years. Screening and identification of behavior problems at earlier ages could make possible initiation of intervention, while considering the likely effects of other confounders.

1. Introduction

Earlier reports suggested an association between prenatal cocaine exposure (PCE) and neonatal malformations and medical complications [18,21,53,61]. However, subsequent studies failed to support such findings [11,55]. Systematic evaluation for congenital anomalies or dysmorphic features revealed no significant association between PCE and minor and major malformations [14,47]. Neither were there differences in the prevalence of cranial abnormalities detected by ultrasound [13]. Therefore, these later studies tempered the rush to judgment that labeled infants with PCE as the “crack kids” of women who were “dangerous” or “unfit to parent” [17,44,69]. However, with experimental findings of PCE affecting brain development [36,60], researchers have continued to evaluate the exposed children to understand the “subtle effects” of in utero cocaine exposure [39]. Animal studies [36,40] showed cocaine effects on brain corticogenesis; i.e., a decrease in the number of cortical cells or proliferation, altered layering of neurons or migration, and changes in the morphology of glial cells. Decreased levels of brain monoamines go with these changes in

corticogenesis [36,40]. Disruption of prenatal development of the monoaminergic system may result in changes in various behavioral processes including emotional regulation or arousal and attention [46]. Indeed, clinical data suggest aberrations in the monoaminergic system [48,50,66] and alterations in behavior [22,25,64] in infants and children with PCE. Reports are however conflicting regarding the effects of PCE on behavior problems at early school-age and preadolescent years. Differences in findings may be attributable to variation in assessments used, number of children assessed, confounders controlled for, and whether the child's parent/caretaker or teacher noted the behavior problems.

Women who use cocaine during pregnancy also use other drugs such as marijuana, opiates, tobacco, and or alcohol. The effects of these substances may confound the long-term effects of PCE on later behavior. Besides prenatal drug exposures, the home environment, caretaker on-going drug use, depression or psychological functioning, neighborhood, exposure to violence and chronic poverty are additional factors reported to be associated with later childhood behavior problems [6,16,68].

We have reported an association between high level of prenatal cocaine exposure and the trajectory of externalizing, internalizing, and total behavior problems through age 7 years as noted by the parent or caretaker [7]. However, the children's behavior in school may differ from behavior manifested at home with the school being a more structured setting and usually with expectations that may vary at different periods within a day. Behavior problems may impair learning and task performance with both requiring more attention and emotional control.

The Maternal Lifestyle Study continues to follow its enrolled children with prenatal exposure to cocaine and or opiate and their comparison cohort. The study assesses its enrolled subjects at intervals in various domains of development including behavior. Thus, in this report, we determined if PCE will predict the trajectory of child's behavior problems from the teacher report, while considering a relationship of ratings between teacher and parent/caretaker as informants. We also determined what other factors other than PCE would predict behavior problems in exposed children. Therefore, we hypothesized that children exposed to high levels of prenatal cocaine are more likely to have higher behavior problem scores as assessed by their teachers in comparison to non-exposed children. We further hypothesized that ratings of behavior problems by the teachers will differ from scores reported by the parents or caretakers.

2. Methods

2.1. Participating sites and study participants

The Maternal Lifestyle Study (MLS) is a multisite longitudinal evaluation of outcomes of children with prenatal cocaine or opiate exposure. This study is ongoing in four collaborating centers: Brown University, Providence, RI; University of Miami, Miami, FL; University of Tennessee, Memphis, TN; and Wayne State University, Detroit, MI. The Research Triangle Institute (Research Triangle Park, NC) and Brown University, respectively, serves as the coordinator for statistics-data management and selection-training for the neurobehavioral battery measures implemented in the study. Each site holds a certificate of confidentiality issued from the National Institute on Drug Abuse and maintains current its approval for research from the Institutional Review Board. A parent or the legally authorized representative gave informed consent; each child also provided assent for participation. Longitudinal follow-up began when the child was one month of age adjusted for prematurity.

Description of our subjects' enrollment and details of follow-up are published [37]. In 1993-1995, the MLS screened neonates for prenatal exposure to cocaine or opiate from 19,079 births across the four participating sites. 16,988 dyads were eligible for a brief maternal interview on drug use and infant meconium testing (Phase1). 11,811 mothers consented to study participation. We identified the exposed children when their mothers admitted to cocaine or opiate use during pregnancy and or their meconium test yielded cocaine or opiate metabolites (n=1185). The non-exposed infants had mothers who denied use of cocaine or opiate during pregnancy and had negative meconium results (n=7442); in 3184 neonates, there was insufficient or no meconium to confirm non-exposure.

2.2. Enrollment of exposed children and comparison cohort in longitudinal follow-up

We selected the subjects for the longitudinal follow-up (Phase 2) from the Phase 1 participants. Of the dyads in the exposed group, 658 of 1185 consented to follow-up and came to the first clinic visit. From the 7442 non-exposed children in Phase 1, we selected the comparison cohort by group matching within site, by gestational age categories, gender, race, and ethnicity and 730 comparison children came to the first clinic visit [45].

2.3. Measures

We categorized PCE into high, some, and no exposure based on a detailed maternal interview at the first follow-up visit. High PCE referred to ≥ 3 times per week use in the first trimester; any other use indicated some cocaine use or some PCE [34,38,59]. We expressed prenatal tobacco exposure as the average number of cigarettes/d, prenatal alcohol use expressed as oz of absolute alcohol/d, marijuana use as the number of joints/d and prenatal opiate use as a yes or no variable.

When the children were 7, 9, and 11 years old, the teachers completed the Teacher's Report Form for Ages 6 -18 (TRF/6-18) [3]; they had no information on the children's prenatal drug exposure. The teacher returned the completed questionnaire by mail to the study coordinator. We derived the T scores for outcomes internalizing, externalizing, and total behavior problems, using a computer scoring system [4]. Internalizing problems include social withdrawal, somatic complaints and anxiety/depression. Externalizing problems include delinquent and aggressive behaviors. Total behavior problems include scales for social, thought, and attention problems that are neither internalizing nor externalizing problems. We also included as outcome attention problems, since PCE effects on the monoaminergic systems are likely expressed as behavioral alterations in attention/arousal [42]. The TRF/6-18 is a parallel form to the Child Behavior Checklist™ (CBCL) [5].

As part of the study's interval assessments, we administered the CBCL to the child's parent or caretaker at similar ages for completing TRF/6-18 and then, at age 13 years. A trained and certified interviewer administered the CBCL verbally during the annual clinic visit to assure uniform administration across four sites regardless of the caretaker's literacy level. We derived the T scores for each behavior outcome using a computer scoring [4]. The CBCL provides a profile of the child's social and behavioral functioning relative to children of the same age and gender. Similar to the TRF, the CBCL also includes the broad band measures for externalizing, internalizing, and total behavior problems and sub-scales including the syndrome of attention problems.

Added measures on the child's caretaker and environment included postnatal caretaker drug use (yes or no), any caretaker experience of physical, verbal, and or sexual abuse or violence (yes or no), and information on income and occupation for each member in the household to derive a measure of socio-economic status (SES), the Hollingshead Index of Social Position [32]. During a home visit when the child was 7 years old, we assessed the child's home

environment using the Home Observation for Measurement of the Environment (HOME) [20]. Other caretaker measures included the Beck Depression Inventory (BDI) [12] with two components of depression (psychological and somatic) administered at the 7-year visit and the Brief Symptom Inventory (BSI) [26] to assess caretaker anxiety and psychological symptomatology, the neighborhood scales, and the Survey of Exposure to Community Violence questionnaire [56] administered during the 9-year visit.

2.4. Statistical Methods

First, we conducted t tests or ANOVA to compare means for continuous variables and Chi-square test to compare proportions for categorical variables. We then performed latent growth curve modeling [29] to determine whether PCE is associated with intercept (baseline values at age seven years) and slope (rate of change over time) of the T scores of externalizing, internalizing, total behavior, and attention problems considering in the model both the TRF and CBCL for years 7, 9, 11 and the CBCL at 13 years.

For each model, we adjusted for multiple covariates. A priori we chose the following covariates: levels of prenatal cocaine exposure, prenatal opiate exposure, levels of other prenatal exposures (tobacco, alcohol, and marijuana), participating sites, child's gender, and maternal age. We further adjusted for other covariates only if the p value overall or any category-wise was ≤ 0.1 . These variables included race, maternal age, and the 7-year visit assessment of postnatal caretaker use (yes/no) of tobacco, alcohol, and marijuana, SES, report of family violence, and caretaker depression (as measured by the BDI), the HOME score [20], and factors examined at the 9-year visit namely: the psychological symptomatology (BSI), neighborhood scales, and survey of community violence. The caretaker's postnatal use of cocaine and opiate was rare for meaningful inclusion in our analyses. Figure 1 outlines our models for the relationship of prenatal cocaine exposure and other covariates to parent and teacher reports of child outcomes, using linear latent growth curve models that include intercept and slope parameters.

We estimated the latent growth curve models with the Mplus software program, specifying the missing data option for maximum likelihood estimation assuming data are missing at random [49]; this approach allowed for inclusion of all children in the analyses. Model fit was assessed using several model fit indices, including the comparative fit index (CFI), Tucker-Lewis fit index (TLI) and root mean square error of approximation (RMSEA). In a linear latent growth curve model, the intercept is the value at the first time point (i.e., 7 years) and the slope is the amount of change from the first to last time points (i.e., change from 7 to 13 years).

3. Results

3.1. Sample characteristics

We enrolled 1388 maternal-child dyads in the follow-up phase of MLS. 1028 (74.1%) had both the TRF and CBCL completed at least one time from 7 to 11 years of age. Table 1 compares the mother-child dyads with and without completed TRF and CBCL. Of those children with evaluation of behavior problems, 79.9% were black compared to 67.2% of those with no assessment ($p < 0.001$). The proportions of PCE, high PCE and opiate exposure were similar between those with and without behavior assessments. Mothers in each group did not differ as to age at the child's birth and in the use of other drugs during pregnancy as to the average number of cigarettes/d, absolute alcohol (oz/d) and number of joints/d of marijuana. Mean birth weight and gestational age did not differ between those children with or without behavioral assessment. A higher percentage of children were discharged from the

nursery to other than their biological mother among those without behavior evaluation, 11.7%, than in those with assessment, 8.1%.

We excluded from analysis children whose mothers admitted to cocaine use in Phase 1 (n=66) but denied use during the detailed interview on enrollment into the follow-up phase, resulting in a total of 962 children included in the analyses. Of the 962 children, 884 (91.9%) had CBCL and/or TRF at 7 years, 905 (94.1%) at 9 years, and 878 (91.3%) at 11 years. The children did not have the TRF-form administered at 13 years but 834 (86.7%) had the CBCL at this age. A total of 730 (75.9%) had measurements for all four years.

3.2. Comparison of teacher and parent ratings

Table 2 presents the means and standard deviations of the T scores for the outcome measures: externalizing, internalizing, total behavior, and attention problems for TRF and CBCL. Teacher's scores were significantly higher for all scores except for attention problems at 9 years ($p=0.803$).

3.3. Latent growth curve modeling

The initial models included levels of prenatal exposures (PCE, tobacco, alcohol, and marijuana), prenatal opiate, maternal age, child's gender, SES, postnatal exposures (tobacco, marijuana, alcohol), BDI, BSI, HOME, family violence, neighborhood scales, and survey of community violence as predictors of intercept and slope of behavior problems observed by the child's teacher and the parent/caretaker. Some variables in the initial modeling did not reach statistical significance at p value <0.10 (postnatal marijuana, BSI, neighborhood scales) and were therefore, dropped from the model. HOME being a direct observation measure, was retained in preference to SES. Reducing the number of predictors improved the parsimony of the latent growth curve models for behavior problems.

Table 3 shows the parameter estimates from the final latent growth curve models investigating the relationship of prenatal cocaine exposure and other covariates to the intercept and slope of the T scores from the TRF and the CBCL for externalizing, internalizing, total behavior problems, and the syndrome of attention problems. All four models fit well: Externalizing (CFI=0.97, TLI=0.93, RMSEA=0.04), Internalizing (CFI=0.96, TLI=0.91, RMSEA=0.04), Total (CFI=0.97, TLI=0.93, RMSEA=0.04), and Attention (CFI=0.98, TLI=0.96, RMSEA=0.03).

3.4. Relationship between parent and teacher reports

As shown in Table 3, the T scores derived from teacher's report were significantly related at baseline (7 years) to ratings by the parent/caretaker for all behavior problems, PCE not withstanding, (parent intercept $\leftrightarrow$ teacher intercept: externalizing problem, $p<0.001$; internalizing problem, $p=0.004$; total behavior problems, $p<0.001$; attention problems, $p<0.001$). The findings suggest that children who were rated poorly by their teachers were also rated poorly by their parents/caretakers or vice versa. However, as noted earlier in Table 2, the scores from teacher report were significantly higher than T scores from the parent CBCL.

There were significant relationships between the changes in scores over time for externalizing, internalizing, total problems, and attention problems between the CBCL and TRF (parent slope $\leftrightarrow$ teacher slope: externalizing, $p<0.001$; internalizing problem, $p=0.005$; total problems, $p<0.001$; attention problems, $p<0.001$).

3.5. PCE and trajectories of behavior problems

Figure 2 shows the estimated growth curves by PCE. After control for covariates, high PCE predicted the intercept for both the TRF and the CBCL externalizing behavior problems, $p<0.034$ and $p=0.021$, respectively. This relationship signifies that externalizing problem scores were higher in children with PCE at 7 years in comparison to non-exposed children, whether observed by the teacher at school or by parent or caretaker at home. PCE, however, did not effect a significant change in externalizing behavior problem scores over time (as indicated by the slope) from observations made by either the teacher or parent/caretaker. The externalizing problem scores remained higher on subsequent years in those exposed to high levels of PCE than those with no PCE.

High PCE did not predict internalizing behavior problems at 7 years from the teacher or parent/caretaker report. PCE, however, marginally predicted total behavior problems at 7 years (intercept) from the TRF ($p=0.063$ and $p=0.063$), respectively for high and some PCE) but was not a predictor of total problems from the CBCL. PCE did not predict the slopes of total behavior problems from TRF or CBCL, suggesting that while children with PCE had more behavioral problems initially, they followed similar trajectories over time, remaining higher than those with no PCE at each time point. High PCE only marginally predicted the parent/caretaker intercept for attention problems. Neither was PCE a significant predictor of the change in attention problems over time (i.e., slopes) from either teacher or parent ratings.

3.6. Prenatal opiate and behavior problems

Prenatal opiate was neither a predictor of teacher nor parent intercepts for outcomes externalizing, internalizing, total behavior, and attention problems. However, there was a significant relationship between prenatal opiate exposure and the slopes of the T scores for internalizing and total problems from the parent report (both p values <0.02), and attention problems from both TRF ($p=0.012$) and CBCL ($p=0.015$). Therefore, although we found no differences between those with and without prenatal opiate exposure at 7 years of age, the opiate exposed children had significant increase in T scores for internalizing, total, and attention problems over time (slopes) in comparison to children with no opiate exposure.

3.7. Other predictors of behavior problems as reported by parent/caretaker

The other significant predictors of CBCL externalizing behavior intercept included postnatal tobacco exposure, caretaker depression, and the child's exposure to community violence. Also, postnatal tobacco, caretaker depression, and community violence predicted the intercepts of internalizing, total, and attention problems from the CBCL. Postnatal alcohol use also predicted internalizing behavior at 7 years. Male gender was a significant predictor of the intercepts of internalizing and total behavior problems by the CBCL. But the only common significant predictor of the CBCL slope for all the behavior problems, including attention problems, was BDI. The slope indicated a minimal decrease in rate of change in behavior problems' T-scores, as the children became older. Given that BDI was also strongly related to behaviors at 7 years based on parent reports (i.e., parent intercept), the smaller change in problem behaviors over time for parents who are depressed (i.e., smaller parent slopes) may be indicative of a ceiling effect.

3.8. Other predictors of behavior problems from the teacher report

HOME and community violence were significant predictors while young maternal age and male gender were marginal predictors of the intercept of the externalizing behavior problem from the teacher report ($p=0.088$ and $p=0.070$, respectively). HOME and male gender also significantly predicted the intercepts of internalizing, total, and attention problems from the TRF. Postnatal alcohol was a marginal predictor of total problems from the TRF. Only

postnatal alcohol exposure predicted the slope of attention problems aside from prenatal opiate exposure.

4. Discussion

4.1. Pertinent findings of the study

This study is the first report on behavior problems determined from observations of cross-informants, i.e., the teachers and parents/caretakers, involving preadolescent children with PCE. Overall, the behavior problem scores as reported by the teachers were higher than scores reported by parents/caretakers at 7 years of age and were consistently higher over time. We also found that high level of PCE predicted externalizing behavior problems, whether the informant was the teacher or parent/caretaker. Children with high PCE had significantly greater externalizing problems at 7 years of age. The rate of change in externalizing problem T scores did not differ significantly by PCE, suggesting that the gap between those with high PCE versus no PCE remained consistent through the subsequent years. PCE was not a significant predictor of total and internalizing behavior by either the TRF or the CBCL. Behavior problems as reported by teacher or caretaker were predicted by other factors, including other drug exposures, family influences, and community factors.

4.2. PCE and externalizing behavior

Evident from the review by Dixon and others [27] on the challenging behaviors of children following prenatal drug exposure were the conflicting reports on the effects of PCE on behavior problems and specifically externalizing problems. The inconsistencies in findings may be related to differences in establishing drug exposure status, children's ages at testing, the small number in some studies minimizing the power to control for confounders, differences in assessment measures (questionnaire versus direct observation), relationship of the informant to the child when the questionnaire was administered, and reporting on cross-sectional versus longitudinal assessments. In our study, in addition to the large number of subjects enrolled, we had repeated behavior outcome measures, and obtained information from both teacher and parent when children reached school age. Specifically, in our cohort, high PCE predicted the trajectory of externalizing behavior problems based on both teacher and parent/caretaker report. Although scores derived from the TRF were higher than scores from the CBCL, the trajectory of the externalizing behavior problem from the TRF paralleled the trajectory from the CBCL.

Few studies evaluated behavior problems in children with PCE with the teacher as the informant; those studies all provided cross-sectional results. Savage and co-investigators [57] found that the teachers reported no difference in behavior problems between cocaine-exposed and non-exposed children at age 10 years. With the use of similar instrument (TRF-6/18) as in our study and after confounders were controlled for, one study noted that PCE was no longer a significant predictor of externalizing behavior; instead, PCE predicted externalizing–internalizing behavior problem difference, a measure of uncontrolled behavior in children with low anxiety [24]. The study also found that a higher percentage of boys had clinically significant externalizing problems in comparison to girls; also, the proportion with clinically significant externalizing behavior problems was twice as high in boys with PCE in comparison to boys with no cocaine exposure [24,51]. In the presence of other prenatal exposures, PCE predicted externalizing behavior only in girls with no prenatal alcohol exposure [51]. In our cohort, gender had a marginal effect on externalizing behavior problem scores based on the teacher report with higher scores in boys than girls and this effect remained constant on subsequent years.

Reports on PCE effect on externalizing behavior with parent/caretaker as the informant, are as conflicting as reports from teachers. Those studies that found no PCE effects related behavior outcomes to environment, maternal depression, or postnatal drug use by caretaker [1,15,54]. Based on parental report prenatal alcohol exposure and gender [62] moderated the effect of PCE. Among girls with no prenatal alcohol exposure, any PCE increased the odds by 17-fold for having scores in the clinical range in aggression (a sub-scale of externalizing behavior problems) in comparison to girls with no PCE. Even after controlling for covariates, we failed to find gender effect for the outcome externalizing behavior problems based on the parent report but found predictability of externalizing behavior problems with postnatal tobacco use, caretaker depression, and exposure to community violence.

4.3 PCE, total behavior, and attention problems

PCE had a marginal effect on total behavior problems from the teacher report in our cohort but not from the parent/caretaker report. However, Kable and co-investigators [35] with the parent as the informant, reported on higher total behavior problem T scores in 8-year old children with PCE in comparison to controls. The behavior problem syndromes included in the total behavior problems and not categorized with externalizing or internalizing problems are social, thought, and attention problems. Within a school's structured setting, teachers are in a unique situation to evaluate children for attention, as well as for their social interactions, thought processes, and ideas.

We also found only a marginal effect of high PCE on attention problems by the parent report. Studies that evaluated attention and arousal in children with PCE found attention deficit and problems with impulsivity even at an earlier age [10] [25]. Bandstra et al. [10] in a longitudinal evaluation of children from 3 years to age 7, found decrements on measures of sustained attention in children with PCE. In another report, children with PCE had more errors of commission in tasks that required more attention and impulsivity control [57]. Children with PCE also demonstrated slower visuomotor speed than control children suggesting impairment in their procedural learning [58]. During imaging studies using diffusion tensor imaging, cocaine-exposed children performed significantly slower on the visual-motor set shifting task [67]. Additionally, physiological responses may be altered in children with PCE. In studies with direct laboratory observation, exposed children in comparison to controls had accelerated physiological response to cognitive and social challenges, as determined by skin conductance levels [35]. These studies of child behavior from observations by teacher and or parent/caretaker and from direct laboratory testing coupled with alterations in physiological responses highlight the complexity of behavioral control in children. A better understanding of all these inter-relationships would be very important since an aberrant behavior could impair academic achievement of these children.

4.4. Prenatal opiate exposure and behavior problems

Most studies of prenatal opiate exposure reported on alterations in neurobehavior within a few days of birth and manifestations were attributed to withdrawal from in utero exposure to narcotics during fetal life [8]. However, follow-up studies found subtle or minimal differences between exposed and non-exposed children in the first few years of life [19]. At ages similar to our follow-up subjects, opiate-exposed children had lower cognitive functioning and more behavioral irregularities than control children [23,33,52]. In our cohort, that prenatal opiate exposure did not predict the intercepts of internalizing, total, and attention problems from parent ratings but T scores increased significantly at later ages (slopes) demonstrates the complex relationship between biological risk of prenatal exposure and child's environment. Other investigators reported that continuing opiate use increased the odds of behavioral problems such as attention deficit and hyperactivity [19].

4.5. Other predictors of behavioral problems

Of the many covariates in our models, caretaker depression and exposure to violence predicted the trajectories of behavior problems from the CBCL. The effects of these factors were independent of the effect of PCE on behavior problems. Depressed caretakers may have over-reported their children's behavior problems; however, studies have indicated that even after accounting for a possibility of error in rating children's behavior, significant association existed between caretaker depression and child behavior problems [30]. In younger children, maternal depressive symptoms but not PCE predicted externalizing and internalizing behavior problems [16]. Others reported that even after considering the effect of PCE and quality of the child's living condition, caretaker depression remained a significant predictor of behavior problems, specifically conduct problems, impulsivity, and hyperactivity [68]. Caretaker depression may result in difficulties in parenting. Impaired engagement and negativity toward the child could lead to difficulties in a child's adjustment to environmental stress and behavior problems [28,63]. Depression becomes more important in parenting in families affected by drug use [31], especially when the infant with PCE may already have neurobehavior alterations thereby further compromising parent-infant interaction [65].

Depression is one of many psychological manifestations in cocaine using mothers. In one report, maternal psychological functioning highly predicted behavior problems in children with PCE [1]. Even in the absence of any prenatal drug exposure, caretaker psychological functioning may serve as a mediator in the path between community violence and childhood behavior problems in children from high-crime neighborhood [41].

Community violence is another risk for aberrations in child behavior. The child's witnessing of violence is a predictor of externalizing, internalizing, and total behavior problems among children with in utero cocaine exposure [6]. In our study, exposure of our children to violence was a highly significant predictor of all behavior problems, more significant than PCE and its effect remained stable through later ages.

The HOME, a measure obtained by direct observation during a home visit, also predicted all behavior problems as reported by the teacher. The child's home environment is also highly related to the caretaker's socioeconomic status, changing when caretaker or custody changes. Change in custody has been reported to predict externalizing behavior from teacher rating among cocaine-exposed children [24]. In early childhood, multiple changes in caretaker create instability in a living situation which negatively impacts a child's adaptive and behavior outcomes [9].

4.6 Stability of behavior problems at school age

The stability of PCE effects on the externalizing behavior problem trajectory at school age raises the question of whether children with problems may be helped with intervention. Unfortunately, our study was not designed to determine the effectiveness of intervention. Our findings, however, should encourage design of intervention studies. From our previous report [7], children with high PCE had higher behavior problem scores (from the parent/caretaker report) even as early as 3 years of age. Future studies will need to target early intervention strategies that may likely minimize or attenuate later childhood behavior problems.

5.0 Study limitations

The large number in MLS and the multiple covariates controlled for in our study enabled us to improve on limitations encountered in previous studies. However, our results can by no means establish causality between PCE and preadolescent behavior problems. Translational

and laboratory studies need to pursue examining various mechanisms underlying behavioral alterations noted with PCE [43] and the possible interaction between the biological risk of prenatal drug exposure and environment. Genetic predisposition and gene-environment interaction were not addressed in this study [43]. Neither did we address the effects of intervention on behavior problems. Our study used broad band measures to assess behavior problems; these instruments lack the details and richness of observations in the laboratory. We recruited our subjects from inner city urban areas with high poverty and crime rates, limiting generalizability of our findings. Studies on children in these neighborhoods showed these children to have problem scores higher than those from the general population [2,5]. Although we used biological measures for detection of prenatal drug exposure [37], we relied on a self report for determination of levels of prenatal and postnatal drug exposures. Under-reporting of drug use may have underestimated the effects of PCE and other drugs. We were unable to determine the effect of postnatal cocaine exposure since a number of children were discharged to other than their biological mothers as guided by state policy regarding newborns with gestational drug exposure.

6.0. Conclusion

High prenatal cocaine exposure is associated with the trajectory of externalizing behavior problems. However, other prenatal and postnatal drug exposures, caretaker characteristics, home environment, and community factors are also risk factors for later behavior problems. Considerations for these factors will be important for successful intervention among children with prenatal cocaine exposure.

Dedication

We dedicate these scientific results to Dr. Vincent Smeriglio and extend our heartfelt thanks for his unwavering dedication and support of the Maternal Lifestyle Study. From the inception and enrollment of the first families more than 15 years ago through the continuing evolution of the study, Vince forever projected an enthusiasm for the continuing search for the long-term impacts of prenatal drug exposure. His thoughtful scientific comments and insights as well as tireless championing for funding assured that the project that was truly a cooperative endeavor. We therefore present the results from follow-up of our cohort through 13 years, finding that prenatal cocaine exposure does have a negative impact on childhood behavior, but is only one of the many risks. Vince's faith, dedication, and interest in the study of prenatal substance exposure on child outcomes provide inspiration to MLS investigators and research staff.

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Data collected at participating sites of the NICHD Neonatal Research Network (NRN) were transmitted to RTI International, the data coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Drs. Abhik Das (DCC Principal Investigator) and Sylvia Tan (DCC Statistician)

had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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Abbreviations

BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
CBCL	Child Behavior Checklist
HOME	Home Observation for Measurement of the Environment
MLS	Maternal Lifestyle Study
SES	socioeconomic status
TRF/6-18	Teacher Report Form for Ages 6 to 18 Years

Figure 1.
Latent growth curve model of change in parent and teacher ratings of behavior problems.

Figure 2.
Estimated linear growth curves for behavior problem T scores from TRF (7, 9, and 11 years) and CBCL (7, 9, 11, and 13 years) by prenatal cocaine exposure.

Table 1

Comparison of dyads with no follow-up and those with child's assessment of behavior problems at least one time from 7 to 11 years of age

Characteristic	No Follow-up (n = 360)	With Follow-up ^a (n = 1028)	p ^b
Race			
Black	242 (67.2)	821 (79.9)	
White	84 (23.3)	136 (13.2)	
Hispanic/other	34 (9.4)	71 (6.9)	<0.001
Marital status: single, n (%)	266 (74.3)	808 (78.7)	0.09
Medicaid, n (%)	284 (78.9)	847 (82.4)	0.16
Education ≤ 12y, n (%)	283 (78.8)	811 (79.0)	0.94
Prenatal cocaine use, n (%)	161 (45.1)	439 (42.9)	0.50
Prenatal opiate use, n (%)	37 (10.3)	78 (07.6)	0.12
High cocaine use, n (%)	33 (10.4)	101 (10.7)	0.92
Prenatal tobacco, mean (SD)	6.6 (10.4)	6.0 (9.3)	0.37
Prenatal alcohol, mean (SD)	0.31 (1.16)	0.30 (0.87)	0.92
Prenatal marijuana, mean (SD)	0.09 (0.41)	0.08 (0.31)	0.58
Maternal age, y, mean (SD)	27.4 (5.8)	28.0 (5.8)	0.07
Child gender: male, n (%)	202 (56.1)	524 (51.0)	0.10
Child's gestation, wk, mean (SD)	36.4 (3.9)	36.2 (4.1)	0.51
Child's birth weight, g, mean (SD)	2682.1 (812.7)	2611.5 (820.2)	0.16
Discharge to other (not biological mother), n (%)	42 (11.7)	83 (8.1)	0.04

^a had teacher report form administered in at least 1 visit at years 7,9, or 11, and known levels of PCE exposure.

^b comparisons between no follow-up and those with school follow-up within the longitudinal sample.

Table 2

Mean parent and teacher ratings (T scores) by age of assessment.

Score/Year	Parent Mean (SD)	Teacher Mean (SD)	P
Externalizing			
7 years	54.77 (11.35)	57.45 (11.51)	<.001
9 years	52.25 (12.10)	56.63 (11.28)	<.001
11 years	54.57 (11.37)	57.95 (10.75)	<.001
13 years	53.53 (10.57)	--	--
Internalizing			
7 years	51.50 (10.24)	52.95 (10.63)	.022
9 years	49.75 (11.09)	52.72 (10.40)	<.001
11 years	51.29 (10.54)	53.62 (10.67)	<.001
13 years	49.86 (10.24)	--	--
Total			
7 years	54.78 (11.41)	56.87 (11.54)	<.001
9 years	52.06 (12.75)	56.01 (11.47)	<.001
11 years	53.46 (11.51)	57.00 (11.30)	<.001
13 years	53.09 (10.92)	--	--
Attention			
7 years	57.84 (8.96)	58.89 (9.68)	.019
9 years	57.86 (8.94)	57.85 (8.70)	.803
11 years	57.23 (8.06)	58.18 (8.22)	.004
13 years	56.98 (7.40)	--	--

Table 3
Parameter Estimates from Latent Growth Curve Model of Change in Behavior From Parent and Teacher Ratings

Path	Externalizing		Internalizing		Total		Attention	
	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P
Growth Curve Parameters								
Parent Intercept ↔ Teacher Intercept	35.86 (4.01)	< .001	8.98 (3.12)	.004	30.46 (3.96)	< .001	28.42 (2.80)	< .001
Parent Slope ↔ Teacher Slope	3.61 (0.77)	< .001	2.47 (0.88)	.005	3.25 (0.80)	< .001	3.31 (0.53)	< .001
Parent Intercept → Parent Slope	-5.15 (1.62)	.001	-2.50 (1.51)	.097	-3.31 (1.64)	.043	-4.38 (1.02)	< .001
Teacher Intercept → Teacher Slope	-11.93 (5.24)	.023	0.09 (6.12)	.989	-7.43 (5.86)	.205	-7.43 (3.95)	.060
Predictors of Parent Intercept								
Prenatal Exposure								
High cocaine	2.62 (1.24)	.034	1.07 (1.08)	.321	1.64 (1.23)	.182	1.78 (1.00)	.076
Some cocaine	-0.58 (0.97)	.553	-1.70 (0.85)	.044	-1.23 (0.96)	.199	0.06 (0.79)	.938
Alcohol	0.74 (0.44)	.091	0.04 (0.38)	.918	0.59 (0.43)	.177	0.56 (0.36)	.113
Marijuana	2.10 (1.22)	.085	1.36 (1.07)	.202	1.97 (1.20)	.102	1.79 (0.99)	.070
Male	0.41 (0.67)	.535	2.20 (0.59)	< .001	1.78 (0.66)	.008	-0.08 (0.54)	.878
Postnatal tobacco exposure	2.76 (0.85)	.001	1.49 (0.74)	.045	2.48 (0.85)	.003	1.60 (0.69)	.021
Postnatal alcohol exposure	1.26 (0.76)	.098	1.55 (0.67)	.020	1.08 (0.76)	.158	0.10 (0.62)	.878
BDI	0.35 (0.05)	< .001	0.43 (0.04)	< .001	0.43 (0.05)	< .001	0.20 (0.04)	< .001
Home environment	0.00 (0.07)	.986	0.14 (0.06)	.016	0.03 (0.07)	.665	-0.05 (0.05)	.373
Community violence	0.71 (0.10)	< .001	0.65 (0.08)	< .001	0.74 (0.10)	< .001	0.36 (0.08)	< .001
Predictors of Parent Slope								
Prenatal Exposure								
High cocaine	-0.11 (0.43)	.793	-0.60 (0.43)	.159	-0.23 (0.42)	.578	-0.32 (0.34)	.336
Some cocaine	-0.19 (0.33)	.554	-0.13 (0.33)	.696	-0.32 (0.32)	.312	-0.26 (0.26)	.315
Opiate	0.68 (0.43)	.109	1.12 (0.44)	.010	1.00 (0.42)	.019	0.83 (0.34)	.015
Alcohol	-0.18 (0.15)	.227	0.02 (0.15)	.905	-0.14 (0.15)	.346	-0.29 (0.12)	.014
Male	-0.10 (0.23)	.656	-0.42 (0.23)	.066	-0.53 (0.22)	.018	-0.15 (0.18)	.389
Postnatal tobacco exposure	-0.13 (0.28)	.652	-0.02 (0.28)	.937	-0.25 (0.28)	.378	-0.47 (0.22)	.038

Path	Externalizing		Internalizing		Total		Attention	
	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P	Estimate (SE)	P
BDI	-0.05 (0.02)	.004	-0.05 (0.02)	.002	-0.06 (0.02)	< .001	-0.04 (0.01)	.006
Community violence	-0.03 (0.03)	.326	-0.06 (0.03)	.090	-0.04 (0.03)	.251	-0.01 (0.03)	.629
Predictors of Teacher Intercept								
Prenatal Exposure								
High cocaine	3.24 (1.40)	.021	1.89 (1.29)	.145	2.61 (1.40)	.063	1.67 (1.18)	.156
Some cocaine	2.49 (1.12)	.026	1.14 (1.03)	.272	2.09 (1.12)	.062	1.34 (0.94)	.154
Opiate	2.63 (1.48)	.076	-1.10 (1.35)	.416	1.52 (1.48)	.304	-0.13 (1.26)	.917
Alcohol	0.43 (0.50)	.384	-0.78 (0.46)	.086	-0.06 (0.50)	.905	-0.36 (0.42)	.391
Marijuana	2.15 (1.40)	.126	1.04 (1.31)	.427	2.60 (1.41)	.065	1.31 (1.18)	.269
Maternal age	-0.12 (0.07)	.088	0.06 (0.07)	.361	-0.04 (0.07)	.539	0.01 (0.06)	.905
Male	1.39 (0.77)	.070	2.35 (0.71)	.001	2.43 (0.77)	.002	1.55 (0.64)	.016
Postnatal alcohol exposure	-0.30 (0.88)	.734	-1.76 (0.81)	.030	-1.02 (0.87)	.244	-1.13 (0.74)	.125
Home environment	-0.15 (0.07)	.041	-0.20 (0.07)	.004	-0.23 (0.07)	.002	-0.20 (0.06)	.001
Community violence	0.22 (0.11)	.047	0.00 (0.10)	.982	0.12 (0.11)	.282	-0.03 (0.10)	.757
Predictors of Teacher Slope								
Prenatal Exposure								
High cocaine	-1.17 (0.83)	.156	-1.50 (0.93)	.107	-0.75 (0.87)	.393	-0.13 (0.71)	.859
Some cocaine	-0.64 (0.66)	.329	-0.64 (0.74)	.389	-0.89 (0.69)	.201	-0.62 (0.57)	.277
Opiate	-0.10 (0.87)	.908	1.53 (0.96)	.112	1.30 (0.91)	.152	1.89 (0.75)	.012
Male	-0.79 (0.46)	.083	-0.26 (0.52)	.617	-0.45 (0.48)	.354	-0.58 (0.40)	.139
Postnatal alcohol exposure	0.19 (0.52)	.721	0.78 (0.60)	.188	0.87 (0.55)	.113	1.10 (0.45)	.014

Note: N=962 (66 from 1028 - excluded from analysis, see text); Due to space considerations, only results for cocaine variables and any variables with $p < .10$ for at least one of the scales are shown. Intercept is the starting value at 7 years of age and slope is the change over time. Due to space considerations, only results for cocaine variables and any variables with $p < .10$ for at least one of the scales are shown. Model fit indices are: Externalizing (CFI=0.97, TLI=0.93, RMSEA=0.04), Internalizing (CFI=0.96, TLI=0.91, RMSEA=0.04), Total (CFI=0.97, TLI=0.93, RMSEA=0.04), and Attention (CFI=0.98, TLI=0.96, RMSEA=0.03).