Children's Cognitive-Behavioral Functioning at Age 6 and 7: Prenatal Drug Exposure and Caregiving Environment

Prasanna Nair, MBBS, MPH; Maureen M. Black, PhD; John P. Ackerman, PhD; Maureen E. Schuler, PhD; Virginia A. Keane, MD

Objective.—The aim of this study was to examine how prenatal drug exposure (PDE) and caregiving environment relate to cognitive, academic, and behavioral performance at ages 6 and 7.

Methods.—A longitudinal follow-up was conducted of 111 children with PDE and a community cohort of 62 non–drug-exposed children (N = 173). Children completed standardized tests of cognition (Stanford-Binet Intelligence Scales, Fourth Edition [SB-IV]) and academic performance (Wide Range Achievement Test 3). Caregivers completed ratings of child behavior problems (Child Behavior Checklist [CBCL]). Multivariate analyses were conducted, adjusting for gender, prenatal tobacco exposure, number of caregiver placement changes, and 3 caregiver variables assessed at age 7, including depressive symptoms, employment status, and public assistance status.

Results.—After adjusting for perinatal and environmental variables, there were no significant exposure-group differences

rug abuse among women of childbearing age is a serious public health problem. Most of the research on the effects of prenatal drug exposure (PDE) has been conducted among young children; findings on performance during the school-age years have been mixed. Some investigators have found no associations between PDE and cognitive performance,^{1,2} play behavior,³ academic achievement,^{2,4} attention, or teacher-rated classroom behavior.² In contrast, others have found associations between PDE and behavior problems,^{1,5} symptoms of oppositional defiant disorder and attention-deficit/hyperactivity disorder,⁶ aggression,⁷ task persistence and attention problems,^{8,9} and language performance.¹⁰ The inconsistent findings may be partially attributed to methodological inconsistencies and to failure to control for confounders, ranging from prenatal tobacco and alcohol exposure¹¹⁻¹⁴ to parental and family variables, such as mental health, education, intelligence, and income. To ensure that variables contributing to children's functioning were identified

in cognition, academic performance, or behavior problems. In comparison with males, females had higher scores on overall IQ and 4 of 8 SB-IV subtests, fewer caregiver-reported attention and aggression problems, and higher reading achievement scores. There were no significant gender-by-group interactions.

Conclusion.—When analyses were adjusted for perinatal and environmental variables, most associations between PDE and cognitive-behavioral functioning were attenuated. Regardless of drug exposure history, males performed more poorly than females on multiple cognitive-behavioral indices. Both exposed and nonexposed children were from low-income families and obtained scores substantially below normative expectations.

KEY WORDS: gender; low income; prenatal drug exposure; school age children

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and controlled, this investigation was guided by developmental-ecological theory,¹⁵ utilizing a bidirectional model whereby children are influenced by their proximal environment, including their family, peers, and schools, and in turn, impact their proximal environment through their behavior.

Investigators have reported that effects of PDE on children's cognitive and behavioral functioning are moderated by gender, with males displaying more adverse behavioral and academic outcomes than females.^{7,16–19} Males are typically exposed to more violence than females, and socially approved male role models are often aggressive, suggesting that social learning may exert an influence in the development of behavioral difficulties.²⁰ Neuroimaging studies have described gender-specific differences in children's brain development, thought to be guided by genetic and hormonal changes as early as the second trimester.²¹ Differences include overall volumetrics, right greater than left frontal asymmetry, and white and gray matter ratios.^{22,23} These differences may explain the lag that males experience in verbal development and their risk for language-related learning disabilities.²⁴

This study examines children with confirmed PDE, defined by positive toxicology and self-report of frequent use, and a nonexposed group of children from the same community. We hypothesize that children with PDE have worse scores on scales assessing cognitive, academic,

From the Department of Pediatrics, Division of General Pediatrics (Dr Nair, Dr Schuler, and Dr Keane), and Division of Growth and Nutrition (Dr Black and Dr Ackerman), University of Maryland School of Medicine, Baltimore, Md.

Address correspondence to Prasanna Nair, MBBS, MPH, 737 West Lombard Street, Room 116, Baltimore Maryland, 21201 (e-mail: pnair@peds.umaryland.edu).

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and behavioral performance compared with children with no exposure. We also hypothesize that males are more vulnerable to the negative effects of PDE than females, as evidenced by worse scores.

METHODS

Study Design and Participants

The participants were part of a longitudinal randomized controlled trial of a home-based intervention among drugusing women and their infants. Recruitment procedures and the home intervention protocol have been reported previously.²⁵ Women were recruited from a university hospital that serves a largely inner-city, African American population. Eligibility criteria included positive maternal or infant urine toxicology screen at delivery or history of substance abuse, gestational age >32 weeks, birth weight >1750grams, and no congenital or medical problems requiring admission to the neonatal intensive care unit. These criteria were imposed so we could evaluate the impact of an early intervention program on children's development without considerations imposed by severe intrauterine growth restriction, congenital problems, or the need for other interventions. Recruitment began in 1991 and continued for 30 months. Women with a history of drug use were approached shortly after delivery; 265 completed the baseline evaluation 2 weeks postdelivery and were randomized into intervention or control groups. The intervention group received biweekly developmentally oriented home visits by a community-experienced outreach worker for 1 year, based on the Infant Health and Development Program.²⁶ The control group received brief monthly tracking visits. Mothers and children were followed for evaluation visits at regular intervals. Data were collected by research assistants blind to intervention status. Mothers were paid for evaluation visits.

At age 7 years, 128 children (48.3%) were available for assessment. Causes of attrition were death 8 (3.0%), foster care placement 37 (14.0%), moved out of state or family withdrew 9 (3.3%), and noncompliance 83 (31.3%). Women lost to follow-up were younger than women who were retained (aged 26.2 vs 27. 7 years; P = .01). There were no differences in neonatal characteristics, maternal drug use, urine toxicology, or other demographic variables.

To ensure that children in the PDE group were exposed to illegal substances prenatally, we used self-report and toxicology screens. Children were assigned to the PDE group if their mother admitted using cocaine and/or heroin at least twice a week for the final 6 months of pregnancy or if the child or their mother had a positive toxicology screen for heroin or cocaine. Children of mothers who reported infrequent drug use throughout pregnancy and who did not have a positive toxicology screen were excluded from analyses (n = 15). Two children within the PDE group were HIV infected and were excluded. Of the final eligible sample of 111 children with a history of PDE, 12.5% of mothers did not have a positive toxicology screen for cocaine or heroin but admitted to frequent use during pregnancy. Of those with positive toxicology screens, 33.3% were positive for cocaine only, 16.2% were positive for heroin only, 50.5% were positive for both cocaine and heroin (Table 1).

Participants in a nonexposed community cohort group served as a community standard for comparison. They were recruited from the university primary care clinic when they were 5 years old. Records were reviewed to identify children who had been born in the university hospital, both the mother and infant had negative toxicology screens (administered routinely at all deliveries) and had no history of drug use. We identified 120 eligible participants and 70 (58%) enrolled. There were no differences in demographic characteristics between those who did and did not enroll. Participants resided in the same community as participants from the PDE group and were matched for socioeconomic status, age of first pregnancy, and race. Sixty-two of the 70 children (89%) from the community cohort group were assessed at age 7.

Children in the PDE group had significantly lower birth weight, length and head circumference, had more neonatal problems, and stayed longer in the hospital compared with the community cohort group (Table 1). The groups differed in exposure to both illicit (eg, heroin and cocaine) and legal substances (eg, tobacco).

Caregivers in the PDE group were significantly older than caregivers in the community cohort group, although there was no difference in age at first pregnancy, caregiver education, or caregiver IQ (Table 1). In comparison with mothers in the community cohort group, caregivers in the PDE group were less likely to be employed, less likely to be married, and more likely to receive public cash assistance. Though groups did not differ in reported current alcohol use, caregivers in the community cohort group reported lower rates of current tobacco and cocaine/heroin use. At age 7, 44.2% of the PDE children were living with nonmaternal caregivers (Table 1); all community cohort children resided with biologic mothers.

Child Measures

Children's cognitive, academic, and behavioral performance were measured by standardized scales with excellent psychometric properties.

Cognition

The Stanford-Binet Intelligence Scales, Fourth Edition (SB-IV) was administered to children aged 6 years.²⁷ The SB-IV assesses intelligence and cognitive abilities and provides an overall test composite score and standard age scores in 4 areas: verbal, quantitative, abstract/visual reasoning, and short-term memory. Raw scores, based on the number of correct items, are converted into standard scores (M = 100, SD = 16).

Academic Achievement

The Wide Range Achievement Test 3 was administered to children aged 7 years and measures basic skills in reading, arithmetic, and spelling.²⁸ Raw scores are converted into standard scores (M = 100, SD = 15).

Table 1. Participant Characteristics by Prenatal Drug Exposure Group and Gender

	Drug H	Exposure Group	Gender				
Neonatal Characteristics	Prenatally Drug Exposed $(n = 111)$	Community Cohort $(n = 62)$	P Value*	Male (n = 78)	Female $(n = 95)$	P Value*	
Birth weight, g [†]	2780 (400)	3380 (570)	<.001	2990 (540)	2930 (530)	.49	
Length, cm [†]	48.0 (2.4)	50.4 (2.6)	<.001	48.9 (2.5)	48.6 (2.9)	.48	
Head circumference, cm [†]	32.7 (1.4)	34.5 (1.6)	<.001	33.4 (1.6)	33.1 (1.7)	.28	
Weight for gestational age, z score [†]	89 (.7)	03 (.9)	<.001	56 (.9)	61 (.9)	.74	
Prenatal drug exposure type							
No prenatal drug exposure		100%		37.2%	34.7%		
Cocaine only	33.3%			19.2%	23.2%	.55	
Heroin only	16.2%			15.4%	6.3%		
Cocaine and heroin	50.5%			28.2%	35.8%		
Tobacco use during pregnancy	84.7%	27.4%	<.001	64%	65%	.90	
Alcohol use during pregnancy	42.3%	30.6%	.14	36%	40%	.67	
Caregiver Characteristics							
Mother's age at first pregnancy [†]	18.6 (4.0)	19.5 (4.2)	.30	19.0 (4.6)	18.1 (3.6)	.24	
Caregiver age [†]	40.3 (9.9)	31.0 (5.5)	<.001	36.2 (8.0)	37.6 (10.9)	.36	
Primary caregiver							
Birth mother	54.9%	100.0%		70.9%	70.8%		
Nonmaternal relative care	44.2%	0%	<.001	29.1%	28.5%	.46	
Nonrelative care	0.9%	0%		0%	0.6%		
Caregiver education [†]	11.4 (1.6)	11.7 (1.1)	.19	11.5 (1.5)	11.5 (1.4)	.89	
Caregiver K-BIT [‡] composite score [†]	81.2 (12.3)	81.7 (10.5)	.78	83.0 (10.5)	80.6 (12.5)	.11	
Caregiver depressive symptoms (CESD)†§	11.7 (9.8)	12.9 (9.9)	.48	12.0 (9.1)	12.2 (10.4)	.89	
Caregiver married	11.5%	19.4%	.18	16.5%	12.5%	.52	
Caregiver public assistance	55.8%	45.2%	.21	54.4%	50.0%	.65	
At least one caregiver employed	65.5%	91.9%	<.001	78.5%	71.9%	.38	
Number of caregiver changes (birth to age 7) [†]	1.1 (1.1)	.03 (.2)	<.001	.7 (1.0)	.7 (1.1)	.96	
Ongoing alcohol use	61.9%	59.7%	.24	67.1%	56.3%	.16	
Ongoing tobacco use	71.7%	33.9%	<.001	57.0%	59.4%	.76	
Ongoing cocaine/heroin use	34.5%	1.6%	<.001	29.1%	17.7%	.10	

*P values are for t statistics when variable is continuous and the chi-square statistic when variable is categorical.

†Mean (standard deviation).

‡K-BIT indicates Kaufman Brief Intelligence Test.

§CES-D indicates Center for Epidemiological Studies Depression Scale.

Behavior

The Child Behavior Checklist (CBCL) was administered to caregivers when children were aged 7 years.^{29,30} The CBCL consists of 120 items related to behavior problems, which are scored on a 3-point scale ranging from not true to often true. Raw scores are converted to t scores (M = 50, SD = 10). The CBCL produces a total behavior problem t score, internalizing and externalizing scales, and several narrow band t scores (eg, anxious/depressed, withdrawn, somatic problems, social problems, thought problems, attention problems, aggressive behaviors, and delinquent behaviors).

Caregiver Measures

The Kaufman Brief Intelligence Test (K-BIT)³¹ was used to measure intellectual ability among caregivers. The K-BIT generates a composite score (M = 100, SD = 15), comprised of verbal and nonverbal abilities. The convergent validity of the K-BIT has been established in a range of populations, including urban, African American populations.

The Center for Epidemiological Studies Depression Scale was used to measure depressive symptoms.³² The 20-item scale addresses 6 aspects of depression: depressed mood, guilt/worthlessness, helplessness/hopelessness, lethargy, loss of appetite, and sleep disturbance. Respondents rate the frequency of symptoms from 0 "rarely or never" to 3 "most or all the time." Higher summed scores indicate more symptoms.

At each evaluation, respondents reported changes in primary caregiver. The number of changes was summed, providing a score representing caregiver changes. Caregivers provided information on their level of education, employment status, whether they were receiving public cash assistance (eg, Aid To Families with Dependent Children, Women, Infants and Children program, or unemployment benefits), marital status, and current substance use derived from the Addiction Severity Index.³³

Statistical Analysis

To identify confounding variables, we examined the intercorrelations among prenatal tobacco and alcohol exposure, infant birth weight for gestational age, number of caregiver changes, and several caregiver variables recorded at the 7-year visit: caregiver education, public assistance status, employment status, depressive symptoms, and ongoing drug use and their associations with PDE and the cognitive-behavioral outcome variables (Table 2).

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. PDE† status		.58***	.12	47***	.48***	.48***	09	.11	28***	06	.37***	15+	13+	12	11	.17*	.02
2. Prenatal tobacco exposure			.26***	38***	.30***	34***	15*	.05	22**	.03	.30***	16*	18*	18*	15*	.16*	.08
3. Prenatal alcohol exposure				12	.05	08	18*	.08	.01	.11	.13+	02	02	05	04	.07	.02
4. Infant birth weight for gestational age					29***	.24**	.08	14+	.23**	.06	22**	.09	.07	.07	02	.04	.04
5. No. of primary caregiver changes (birth to age 7)						63***	21**	.10	23***	.01	.17*	23***	19*	13+	07	.13+	.02
6. Placement in nonmaternal care							.09	12	.26***	.14+	.06	.19*	.08	.06	.05	11	03
7. Caregiver education								19*	.21**	20**	12	.12	.06	.07	.09	05	04
8. Caregiver receives public assistance									29***	.10	.20*	17*	12	14+	10	02	.08
9. Caregiver employment status										01	29***	.17*	.02	.06	.06	.02	02
10. Caregiver depressive symptoms											.09	13+	12	22**	20**	.26***	.41***
(CES-D)‡																	
11. Caregiver ongoing drug use												09	12	11	02	.07	.03
12. Child SB-IV§ total composite													.56***	.55***	.59***	15+	16*
standard score														0.0 *****	Contrativity		0.5 ****
13. Child WRAT3 reading achievement														.88***	.69***	29***	25**
14. Child WRAT3 spelling achievement															.66***	26**	22**
15. Child WRAT3 arithmetic achievement																23**	28***
16. CBCL¶ externalizing behavior problems	6																.67***
17. CBCL internalizing behavior problems																	

Table 2. Correlations Among Demographic and Study Outcome Variables (N = 173)

**P* < .05.

**P < .01.

***P < .001.

†PDE indicates prenatal drug exposure.

CES-D indicates Center for Epidemiological Studies Depression Scale.

§SB-IV indicates Stanford-Binet Intelligence Scales, Fourth Edition.

WRAT3 indicates Wide Range Achievement Test 3.

¶CBCL indicates Child Behavior Checklist.

Covariates were selected based on significant associations with independent and dependent variables of interest. In analyses involving cognitive and academic outcomes, we controlled for gender, prenatal tobacco exposure, number of caregiver changes, public assistance status, employment status, and caregiver depressive symptoms. In analyses on the CBCL, we controlled for gender, prenatal tobacco exposure, number of caregiver changes, and caregiver depressive symptoms. We examined intervention status within the PDE group and found no effects of intervention or intervention by covariate interactions on the cognitivebehavioral variables. Therefore, intervention status was not included in the analyses.

To test the first hypothesis that children with PDE would have lower scores on measures of cognitive, academic, and behavioral performance at age 6 and 7 than nonexposed children, we conducted multivariate analyses of variance, followed by univariate analyses (ANOVA) to identify differences within specific subtests. This strategy reduces the likelihood of a type 1 error that might result from conducting multiple ANOVAs. PDE and community cohort were the independent variables. We began with unadjusted analyses, followed by analyses adjusted for covariates.

To test the second hypothesis, that the effects of PDE were modified by gender, we repeated the analyses and included a gender-by-group interaction term, comparing children in the PDE and community cohort groups. Finally, we analyzed gender as a main effect to examine whether males were more vulnerable than females. According to Cohen,³⁴ a sample size of 128 is required to detect group differences with a medium effect size for a power of 0.80. Thus, this study (N = 173) has adequate power to detect medium and large effect sizes.

RESULTS

Cognition

Unadjusted multivariate analyses indicated that children in the PDE group scored lower than children in the community cohort group on the SB-IV (F [8, 165] = 2.27; P < .05), and more specifically, for the 2 subtests absurdities (F [1, 172] = 5.59; P < .05) and memory for sentences (F [1, 172] = 14.38; P < .001).

After adjusting for covariates, there were no significant differences by exposure group on the overall SB-IV composite score, the 4 area scores, or on individual subtests (Table 3). The gender-by-group interaction was not significant.

There was a main effect for gender (see Table 3) such that males had significantly lower performance than females on the overall SB-IV test composite, 2 of 4 area scores (verbal reasoning and short-term memory), and 4

Table 3. Cognitive and Academic Achievement Outcomes by Exposure Group and Gender

	Drug	Exposure Group	Gender			
Characteristics	Prenatally Drug Exposed ($n = 111$) mean (SD)	Community Cohort (n = 62) mean (SD)	P Value*	Male (n = 78) mean (SD)	Female (n = 95) mean (SD)	P Value*
SB-IV [†] (age 6)						
Subtest						
Vocabulary	43.7 (6.4)	45.4 (6.5)	.45	43.3 (5.9)	45.2 (6.8)	.04
Comprehension	47.1 (6.1)	48.3 (5.7)	.53	45.5 (5.3)	49.2 (6.0)	<.001
Absurdities	43.7 (5.1)	45.5 (4.3)	.49	43.8 (4.9)	44.8 (4.9)	.14
Pattern analysis	42.2 (5.4)	43.0 (6.4)	.99	41.4 (4.9)	43.3 (6.3)	.02
Сору	35.1 (3.9)	35.7 (3.3)	.98	35.3 (3.4)	35.2 (4.0)	.87
Quantitative	44.7 (6.6)	46.4 (8.5)	.80	44.6 (7.4)	45.9 (7.3)	.21
Bead memory	41.2 (7.1)	41.0 (8.3)	.58	40.2 (7.0)	41.9 (7.9)	.15
Memory for sentences	43.2 (4.9)	46.1 (4.7)	.07	43.3 (5.0)	45.0 (4.9)	.01
Standard Area Scores						
Verbal reasoning	88.4 (11.0)	91.3 (11.2)	.46	87.0 (9.6)	91.4 (12.0)	.01
Abstract/visual reasoning	73.8 (9.0)	75.4 (9.3)	.97	73.2 (7.7)	75.4 (10.1)	.13
Quantitative reasoning	89.4 (13.2)	92.7 (16.9)	.80	89.2 (14.8)	91.8 (14.6)	.24
Short-term memory	81.6 (11.7)	84.7 (12.6)	.71	80.6 (11.5)	84.5 (12.3)	.03
Composite standard score (IQ)	80.1 (10.1)	83.3 (11.2)	.81	79.2 (9.5)	83.0 (11.2)	.01
WRAT3‡ (age 7)						
Reading	93.3 (15.9)	97.6 (16.1)	.86	92.2 (16.1)	96.9 (15.9)	.05
Spelling	93.9 (14.7)	97.9 (17.8)	.95	93.2 (16.4)	97.0 (15.5)	.10
Arithmetic	87.4 (17.1)	91.4 (17.0)	.60	86.8 (17.3)	90.5 (16.9)	.14

*All multivariate comparisons between prenatal drug exposure and community cohort groups controlled for gender, prenatal tobacco exposure, number of caregiver changes, caregiver depressive symptomatology, employment status, and public assistance status. In an examination of cognitive differences on the SB-IV, there was not a significant prenatal drug exposure status × gender interaction, nor was there a significant main effect for prenatal drug exposure status (F [8, 165] = 1.16; P = .33). Only child gender was significantly associated with cognitive functioning in the final model (F [8, 165] = 2.88; P = .005). An examination of academic achievement differences on the WRAT3 indicated that there was not a significant prenatal drug exposure status × gender interaction nor was there a significant main effect for prenatal drug exposure status (F [8, 165] = .30; P = .82), or child gender (F [8, 165] = 1.26; P = .28). Caregiver depressive symptomatology (F [8, 165] = 5.30; P = .002) was a significant multivariate predictor of child academic achievement in the final model.

 \dagger SB-IV indicates Stanford-Binet Intelligence Scales, Fourth Edition. Means and (standard deviations [SD]). Subtest mean = 50, SD = 8; Standard area scores mean = 100, SD = 16.

#WRAT3 indicates Wide Range Achievement Test 3. Standard scores. Mean = 100, SD = 16.

of the 8 subtests (vocabulary, comprehension, pattern analysis, and short-term memory).

Academic Achievement

There were no significant associations between exposure group and reading, spelling, or arithmetic achievement by using unadjusted or adjusted comparisons (Table 3). The gender-by-exposure group interaction was not significant. Although there was not a significant multivariate effect for gender on academic achievement, males had significantly lower reading achievement scores than females.

Behavior

Unadjusted multivariate analyses indicated that children in the PDE group were rated as having more behavioral problems than children in the community cohort group on the CBCL (F [8, 165] = 3.30; P < .01), and more specifically, aggression (F [1, 172] = 5.35; P < .05) and externalizing behavior problems (F [1, 172] = 4.95; P < .05).

After adjusting for covariates, there was a significant multivariate main effect for exposure group on caregiver-reported behavior problems on the CBCL (Table 4); however, there were no significant differences on any of the individual subscales or any of the broadband behavioral domains. There was not a gender-by-exposure group interaction.

Males were rated as having more externalizing behavior problems than females (Table 4). Males had significantly higher aggression and attention behavior problem ratings than females as well as marginally higher levels of delinquent behavior problems.

DISCUSSION

This study yielded 3 major contributions to findings related to low-income, urban children with a history of PDE. First, with the inclusion of perinatal and environmental covariates, there were few differences in cognitive, academic, and behavioral performance scores between the children, based on PDE history. These findings are striking because not only did we use maternal affirmation plus positive toxicology screens to confirm PDE status, but we recruited a community comparison group that represented families who resided in the same low-income communities as the PDE children and that had experienced many of the same environmental challenges associated with poverty, but had not experienced PDE or the early caregiver disruptions that frequently occur among drug-using families.³⁵ Our analyses suggested that the perinatal, maternal, and family covariates, selected on the basis of developmentalecological theory, explained more variance in early child functioning than a history of PDE.

Some of the controversial findings in the field of PDE may be related to inconsistent attention to potential confounders. The negative consequences of prenatal exposure to alcohol and tobacco are well known,^{13,14} yet many investigators have not adjusted for them in their analyses. In our bivariate findings, prenatal tobacco use occurred more often in the PDE group than in the community cohort group and was related to children's lower functioning in multiple domains at ages 6 and 7. Thus, ignoring prenatal tobacco exposure could have led us to attribute more negative effects to PDE than warranted.

Substance-using women are at risk for mental health problems, including depressive symptoms that may interfere with their caregiving ability.³⁶ In our analyses, we found associations between caregiver depressive symptoms and measures of children's academic performance and caregiver-reported behavior problems. Again, investigators who have not considered caregiver depressive symptoms may have attributed children's performance patterns to PDE rather than to caregiver report measures.

Table 4. Parent-Reported Behavior Problems by Exposure Group and Gender at 7 Years

	Drug	Exposure Group	Gender			
CBCL*t scores (age 7)	Prenatally Drug Exposed ($n = 111$) mean (SD)	Community Cohort (n = 62) mean (SD)	P Value†	Male (n = 78) mean (SD)	Female (n = 95) mean (SD)	P Value†
Aggressive behavior	51.1 (10.6)	47.5 (8.3)	.09	50.9 (10.6)	49.2 (9.4)	.04
Anxious/depressed	50.5 (10.9)	47.9 (7.7)	.13	50.3 (9.6)	49.4 (9.3)	.73
Attention problems	51.0 (10.8)	48.7 (8.8)	.51	51.9 (11.7)	48.5 (8.2)	.006
Delinquent behavior	50.6 (10.8)	48.3 (7.5)	.84	51.2 (9.7)	48.7 (8.2)	.08
Social problems	50.9 (10.3)	48.7 (9.1)	.60	51.6 (10.8)	48.5 (8.2)	.47
Somatic complaints	49.5 (9.4)	50.5 (10.3)	.75	49.3 (9.6)	50.5 (10.3)	.21
Thought problems	50.2 (10.0)	50.1 (11.0)	.86	50.2 (8.6)	49.9 (10.7)	.61
Withdrawn behavior	49.1 (9.7)	51.2 (10.8)	.15	51.2 (10.6)	49.2 (9.2)	.11
Internalizing problems	49.8 (10.2)	49.4 (9.3)	.84	50.4 (9.2)	49.6 (9.4)	.22
Externalizing problems	51.0 (10.8)	47.6 (8.0)	.19	51.0 (10.5)	49.0 (9.1)	.04
Total behavior problems	50.7 (10.4)	48.3 (8.8)	.28	51.2 (10.8)	48.7 (8.9)	.06

*CBCL indicates Child Behavior Checklist; SD indicates standard deviation. Mean = 50, (SD = 10).

†Multivariate comparisons between prenatal drug exposure and community cohort groups controlled for gender, prenatal tobacco exposure, number of caregiver changes, and caregiver depressive symptoms at age 7 visit. Separate analyses were run for subscales, internalizing and externalizing scores, and the total CBCL score. There was not a significant prenatal drug exposure status \times gender interaction; there was a significant main effect for prenatal drug exposure status (F [8, 165] = 2.48; P = .02). Child gender (F [8, 165] = 2.29; P = .02) and caregiver depressive symptoms (F [8, 165] = 4.85; P < .001) were significant predictors of child behavior problems in the final model.

Children who were born with PDE had lower scores than children in the community cohort group on the total score of caregiver-reported behavior problems, even after adjusting for perinatal and environmental factors. However, the lack of differences on the internalizing or externalizing scales or on any of the narrow band scales suggests that there may have been subtle differences that only reached significance when all behaviors were considered together.

Caution is warranted when interpreting the present findings because there is evidence that PDE may be a risk factor for subtle, specific neurodevelopmental deficits, rather than global deficits. Arousal and attentional systems appear to be particularly vulnerable to the effects of PDE.³⁷ Richardson and colleagues² reported that even when there were no differences between PDE children and a matched comparison group at age 6 years on intellectual ability, academic performance, or teacher ratings, PDE children had deficits in sustained attention. Bendersky and colleagues^{7,38} have provided evidence that exposure to cocaine in utero has a negative effect on inhibitory control functioning and is associated with aggressive behavior problems at age 5. Although other investigations have also found that PDE children display more externalizing and total behavior problems than children with similar backgrounds who were not exposed to drugs prenatally, covariate adjustment has varied.^{5,6,16}

These findings suggest that the effects of PDE must be considered in the context of the home environment.^{3,4,7,15} In an analysis among PDE children at 18 months, we showed that parenting stress and child abuse potential were higher for caregivers with 5 or more risk factors compared with caregivers with fewer risk factors.³⁹ Although at that time children's developmental status did not differ by caregiver risk status, it is possible that sustained exposure to caregivers who find parenting stressful and have an inclination toward abuse or harsh parenting could eventually result in behavioral and developmental problems. Both cocaine-exposed and nonexposed fourth grade children in low-income families have better cognitive functioning and academic performance when they are raised in better functioning homes.⁴ However, in keeping with developmental-ecological theory, findings should be interpreted from a bidirectional perspective. That is, children are not only influenced by their environment, but children influence their environment through their behavior.

A second finding is that males demonstrated more vulnerability than females in 4 of 8 subtests of the SB-IV, the aggression and attention subscales from the CBCL, and reading scores from the Wide Range Achievement Test 3. Effect sizes related to cognitive functioning ranged from small to medium (Cohen's *d*, 0.3–0.6) and were small for behavioral and academic findings (Cohen's *d*, 0.2–0.3).³⁴ These data are consistent with findings regarding vulnerability among males in general, including those prenatally exposed to illegal substances,^{7,16,17,40,41} with deficits commonly noted in sustained attention, concentration, self-regulation, and working memory, skills that are associated with activation of the prefrontal cortex.

Gender differences in brain development occur as early as 18 weeks gestation when males begin producing testosterone, which leads to several hormone-related changes in the brain. Males develop greater hemispheric asymmetry (right hemisphere larger than left), slightly larger overall brain volume, proportionately less gray matter relative to white matter, a thinner corpus callosum, and more cerebrospinal fluid surrounding the brain than females. Although such neuroanatomical differences may contribute to certain advantages for males in spatial abilities and a propensity towards physical action, they may also put males at an increased risk for attention, language, and information processing deficits, because males tend to share information between hemispheres less efficiently than females.^{24,42}

In our data, the absence of gender-by-exposure interactions indicates that the effects of gender and PDE were not synergistic. In other words, males had worse performance than females across several measures of cognition and behavior, regardless of PDE status.

Finally, the children's low cognitive and academic achievement scores, regardless of PDE history, are consistent with findings from other samples of low-income children with and without PDE.^{4,43} Poverty has an insidious effect on multiple aspects of child functioning, particularly when it occurs in the context of maternal depressive symptoms.⁴⁴ Recent evidence from the National Institute of Child Health and Human Development Early Child Care Research Network⁴⁵ has shown that 9-year-old children in chronically impoverished families had lower cognitive performance and more behavior problems than children who were not exposed to poverty, partially explained by a lack of enriching parenting behaviors and home experiences.

Methodological Limitations

There are several methodological limitations that should be considered in interpreting the data. First, although we relied on toxicology screens and self-report of frequent drug use to determine the level of substance exposure, it is possible that there may have been some misclassification among women who used substances early in their pregnancy-but not at the time of delivery- and failed to report substance use. Second, due to the limited sample size and the high prevalence of polysubstance use, we could not detect small, drug-specific differences, and we could not examine whether the severity of exposure was related to children's behavior and development. However, most drug-using women use multiple substances, which makes this a fairly representative sample.^{14,25} Third, we may have eliminated the highest risk infants by including only infants who were relatively healthy at birth. Thus, findings do not generalize to infants with intrauterine growth restriction, prematurity, or congenital problems. Fourth, although the gender differences were consistent with other reports, they were relatively small, raising questions about their clinical significance.

Finally, we limited our control of the caregiving environment to demographic, psychological, and self-report variables. Although we included multiple confounders based on developmental-ecological theory, it is likely that additional environmental variables play a substantial role in children's behavior and academic performance.

Future Directions

In summary, once theoretically and empirically derived confounders were included in the analyses, most differences in the children's cognitive, behavioral, or academic performance at ages 6 and 7 years were attenuated. Future investigations of PDE children should adjust for potential confounders to ensure that attributions to PDE are accurate. In addition, it may be useful to examine subtle aspects of neurocognitive functioning, which may be more sensitive to PDE than global assessments of functioning. It is also possible that performance differences related to PDE could occur as children age and use alternative cognitive and problem-solving strategies.

Low-income children, especially males, are at risk for poor cognitive and behavioral functioning. Interventions are needed to ensure that children in low-income families, regardless of their history of PDE, receive developmentally enriching opportunities early in life to avoid the cognitive and behavioral consequences that can undermine subsequent success.

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