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Impact of Prenatal Cocaine Exposure on Attention and Response Inhibition as Assessed by Continuous Performance Tests

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Abstract

Objective—This study examined the influence of prenatal cocaine exposure on attention and response inhibition measured by continuous performance tests (CPTs) at ages 5 and 7 years.

Methods—The baseline sample consisted of 253 cocaine-exposed and 223 non-cocaine-exposed children enrolled prospectively at birth and assessed comprehensively through age 7 years in the longitudinal Miami Prenatal Cocaine Study. This report includes a subsample of 415 children (219 cocaine-exposed, 196 non-cocaine-exposed) who completed at least one CPT assessment at ages 5 and/or 7 years. Prenatal cocaine exposure was measured by maternal self-report and maternal and infant bioassays. Deficits in attention and response inhibition are estimated in relation to prenatal cocaine exposure using generalized estimating equations within the general linear model.

Results—Results indicate cocaine-associated increases in omission errors at ages 5 and 7 as well as increases in response times for target tasks (i.e., slower reaction times) and decreased consistency in performance at age 7. There were no demonstrable cocaine-associated deficits in commission errors. Estimates did not change markedly with statistical adjustment for selected prenatal and postnatal covariates.

Conclusion—Evidence supports cocaine-associated deficits in attention processing through age 7 years.

Index terms

prenatal cocaine exposure; sustained attention; response inhibition; continuous performance test

Accumulating evidence suggests that prenatal cocaine exposure disrupts arousal and attention regulation in off-spring. In animal models, *in utero* cocaine exposure has been shown to alter the developing monoaminergic system, resulting in both structural and functional changes to circuitry subserving functions such as arousal and attention.^{1,2} Moreover, gestational cocaine exposure produces behavioral responses in animals consistent with altered attention processing, including impairments in selective and sustained attention.^{3–9} Difficulties with

arousal and emotional regulation have also been reported.^{9–11} In several studies, deficits were evident in adulthood, demonstrating potential for long-lasting impairment following *in utero* cocaine exposure.^{5,6,9}

Clinical research with infants and toddlers has also indicated cocaine-associated dysfunction in arousal and attention. Although inconsistent across studies, prenatal cocaine exposure has been associated with poorer autonomic stability, state regulation, orientation, and habituation on the Brazelton Neonatal Behavioral Assessment Scale and similar measures.^{12–14} Infants exposed prenatally to cocaine have also shown more arousal and arousal/affect regulation difficulties on various behavioral and physiological measures.^{15–17} During toddlerhood, prenatal cocaine exposure has been related to greater perseveration and inability to delay gratification on laboratory tasks^{18,19} and poorer examiner-rated emotional regulation and task orientation.¹⁹

These findings support the hypothesis that prenatally cocaine-exposed infants may have increased difficulties with attention and self-regulation in later childhood, but relatively few studies have examined the long-term impact of *in utero* cocaine exposure on aspects of attention and impulsivity during preschool- and school-age years. The Continuous Performance Test (CPT) is a widely used measure of vigilance and response inhibition, and variations of the CPT have been used to capture neurodevelopmental consequences of prenatal substance exposure.^{20,21} Several reports have suggested poorer CPT performance in prenatally cocaine/polydrug-exposed children,^{22–25} although findings should be interpreted in light of methodological limitations noted in some of the studies (e.g., small sample size; failure to control for key covariates; sample attrition).

The Miami Prenatal Cocaine Study (MPCS) was established to evaluate long-term effects of prenatal cocaine/polydrug exposure on children's neuropsychological, emotional/behavioral, and educational functioning. In a previous report from the MPCS, we presented longitudinal evidence of prenatal cocaine-associated sustained attention deficits measured by a standardized assessment of task persistence at age 3 years and CPT omission errors at ages 5 and 7 years.²⁶ This report builds on previously published findings by evaluating the impact of prenatal cocaine exposure on several indicators of attention processing and response inhibition, i.e., CPT omission errors, commission errors, response time variability, and average response time at ages 5 and 7 years. Longitudinal multivariate statistical methods are used to control for potentially confounding influences and examine the statistical independence of cocaine-associated deficits in relation to other postnatal factors, such as maternal/caregiver drug use.

METHODS

Study Participants

Participants were children and their caregivers enrolled in the Miami Prenatal Cocaine Study (MPCS). The originating cohort consisted of 253 cocaine-exposed (with or without exposure to alcohol, tobacco, or marijuana) and 223 comparison infants, of whom 147 were drug free and 76 were exposed to varying combinations of alcohol, tobacco, or marijuana. The study sample was homogeneous with regard to full-term gestation (≥ 37 weeks), low socioeconomic status, inner-city residence, and African-American ethnicity. Exclusion criteria were maternal HIV/AIDS; prenatal exposure to opiates, methadone, amphetamines, barbiturates, benzodiazepines, or phencyclidine; major congenital malformation; chromosomal abnormality; or disseminated congenital infection.

The current report focuses on the hypothesized impact of prenatal cocaine exposure on CPT performance. Analyses are based on a subsample of 415 children (219 cocaine-exposed, 196 non-cocaine-exposed) who completed at least one standardized CPT assessment at ages 5 and/

or 7 years. Table 1 presents selected maternal and child characteristics measured at birth for this study sub-sample.

Study Design

The overall study design and recruitment of the follow-up cohort for the longitudinal MPCs, briefly summarized here, has been detailed elsewhere.²⁷ The study was approved by the Institutional Review Board and conducted under a Department of Health and Human Services Confidentiality Certificate.

Participants were recruited at delivery from the University of Miami-Jackson Memorial Medical Center (UM-JMMC) from November 1990 through July 1993. The MPCs follow-up cohort ($n = 476$) was drawn from a larger survey of mothers and infants delivering at term gestation ($n = 1,505$). Of the mothers participating in this survey of drug abuse, 154 were determined ineligible for the follow-up due to positive or unknown maternal HIV status, and an additional 25 participants were excluded due to heroin or other drug exposure (not including alcohol, tobacco, and marijuana). From the remaining eligible full-terms ($n = 1,326$), participant selection and study group assignment occurred as follows. Prenatal cocaine exposure was identified by maternal self-report or a positive biological marker (i.e., maternal urine, infant urine, and/or infant meconium). Cocaine-exposed infants also had varying levels of exposure to alcohol, tobacco, and marijuana. Eighty-nine percent of the eligible cocaine-exposed infants were enrolled in follow-up. Non-cocaine-exposed drug-free infants met the following criteria: negative maternal lifetime history for cocaine use, negative self-report for any drugs of abuse during pregnancy and the 3 months before pregnancy, and negative toxicology results on all available specimens. As the number of infants meeting these criteria exceeded the target recruitment number, a random numbers table was used to balance recruitment of drug-free infants across the study period. The comparison group was designed to also include non-cocaine-exposed infants exposed to alcohol, tobacco, and/or marijuana, determined by a positive self-report for alcohol, tobacco, or marijuana use during pregnancy or a positive biological marker for marijuana. An emphasis was placed on enrolling those mothers with a minimum ingestion criterion of 20 drinks of alcohol during pregnancy. Eighty percent of the non-cocaine-using mothers meeting this criterion were enrolled in the comparison group.

Data Collection Procedures

Pertinent medical and demographic information were collected from the medical records at birth. Caregiver and child data relevant to the present study were drawn from serial neurodevelopmental assessments conducted at 5 and 7 years. Examiners blinded to substance exposure status performed all child assessments.

Drug Exposure Measures at Birth

Trained research staff conducted a structured postpartum interview to ascertain maternal substance use and additional demographic information. To enhance recall, targeted periods were anchored to important calendar dates. Gestational drug use questions were asked by trimester, and dose was measured in number of cigarettes, marijuana joints, standard alcoholic drinks, and cocaine lines/rocks. Standardized definitions were used for one-drink units for beer (12 oz.), wine (5 oz.), and liquor (1.5 oz.).²⁸ Pregnancy exposure composites for each drug, calculated by multiplying the number of weeks used by the usual days per week and the usual dose per day, are presented in Table 2. Exposure composites for alcohol, tobacco, and marijuana were used as covariates in analyses.

Screening for cocaine metabolite (benzoylecgonine) was performed by EMIT® (Syva D.A.U.), at a cutoff of 150 ng/mL urine and 150 ng/g meconium, respectively; cocaine-positive

specimens were confirmed by gas chromatography/mass spectrometry.²⁹ EMIT® was also used for urine assays of marijuana (cannabinoids), opiates, amphetamines, barbiturates, benzodiazepines, and phencyclidine and meconium assays of marijuana and opiates.

Child Measures

Continuous Performance Test Measures—Continuous performance tests (CPTs) were administered at approximately 5 and 7 years. At age 5, the Test of Variables of Attention (TOVA) CPT,³⁰ a non-language-based CPT normed for individuals 4 through 80+ years, was given. In this task, the child presses a micro-switch to identify a target stimulus from two easily discriminated geometric figures (target and non-target stimulus) presented randomly on the computer screen. A stimulus appears every 2 seconds and is displayed for approximately 100 milliseconds. For children younger than age 6, test duration is 10.8 minutes. An instructional practice phase precedes the actual task, which requires no right-left discrimination and has negligible practice effects. The TOVA has shown sensitivity to medication effects in attention-disordered children as young as 5 and 6 years of age^{31,32} and has demonstrated good sensitivity and specificity in discriminating attention disorders from other psychological disorders and from normal functioning in school-age children^{33,34} (Greenberg and Crosby, unpublished, 1992, available from Universal Attention Disorders, Los Alamitos, CA).

The Conners' Continuous Performance Test (Conners')³⁵ was given at 7 years. The Conners' (14 minutes) was administered instead of the school-age TOVA (23 minutes) due to concerns regarding the duration of the overall testing day. In this task, large bold-faced letters are presented at intervals between 1 and 4 seconds and displayed for approximately 250 milliseconds. Participants are instructed to press the space bar for all letters except X. Normative data are available for individuals from 4 to 61 years of age. The Conners' has been shown to distinguish between individuals diagnosed with attention-deficit/hyperactivity disorder (ADHD) from the general population and has shown good sensitivity to treatment effects.³⁵ Omission errors, commission errors, correct response times, and response time variability raw scores from the TOVA and Conners' were analyzed. Table 3 describes the eight CPT variables under study.

To provide evidence of convergent validity for the CPT indicators as measures of sustained attention and impulsivity in this sample, each indicator was correlated with measures of similar constructs, i.e., the Attention Sub-scale from the parent-report Achenbach Child Behavior Checklist (CBCL)³⁶ administered at 5 and 7 years and the Attention/Executive Function domain from the NEPSY: A Developmental Neuropsychological Assessment³⁷ administered at 7 years. TOVA Omission and Standard Deviation of Response Time scores were modestly correlated with the 5-year CBCL Attention Problems Subscale score ($r = 0.11, p = .04$; $r = 0.14, p = .01$), and all TOVA indicators were associated with performance on NEPSY Attention/Executive Function domain at age 7 ($r = -0.13$ to $-0.33, p < .02$). Similarly, the Conners' Omission score was correlated with 7-year CBCL Attention Problems Subscale Score ($r = 0.11, p = .03$), and all Conners' CPT indicators were significantly correlated with the NEPSY ($r = -0.12$ to $-0.36, p < .02$). CPT performance was also associated with academic achievement, measured at age 7 by the Wechsler Individual Achievement Test (WIAT) Screener Composite Score,³⁸ with correlations between the WIAT and the TOVA indicators ranging from $r = -0.13$ to $-0.28 (p < .02)$ and the Conners' indicators ranging from $r = -0.13$ to $-0.20 (p < .01)$.

Intellectual Functioning Measure—The Full Scale IQ from the Wechsler Scale of Preschool and Primary Intelligence-Revised,³⁹ administered at age 5 years, was entered in analyses to examine whether the hypothesized association between *in utero* cocaine exposure and CPT performance was independent of cognitive ability.

Postnatal Caregiver Measures

Psychosocial Interview—A structured psychosocial interview was conducted with each child's mother/primary caregiver at the 5- and 7-year visits. Biological mothers residing with and parenting the child were prioritized for interview purposes as the primary caregiver. The primary caregiver was otherwise defined as the family member or custodial guardian responsible for the child's physical, emotional, and financial well-being. Table 4 summarizes selected postnatal factors assessed by these interviews. Past year caregiver drug use variables include only alcohol, marijuana, tobacco, and cocaine due to the relatively low rate of other drug use. Terms for postnatal characteristics measured at the 5-year visit were included in the models to assess the relationship between prenatal cocaine exposure and CPT performance with these factors held constant.

Statistical Analyses

After examining initial descriptive statistics and longitudinal plotting, the longitudinal influence of prenatal cocaine exposure as a dichotomous indicator (yes/no) was evaluated in relation to the selected indicators of attention and response inhibition at 5 and 7 years using generalized estimating equation (GEE) procedures within the general linear model (GLM), a flexible working correlation structure, and robust estimation of SEs under STATA, Version 8.^{40,41} This approach was motivated by interest in a population-averaged estimate of the hypothesized effect of prenatal cocaine exposure on attention processing and by regression diagnostic results indicating departures from the compound symmetry assumption required for repeated-measures analysis of variance. In addition, this approach allowed for utilization of all available data at each age point, unlike repeated-measures analysis of variance, which limits case inclusion by requiring data availability at all age points under study. The primary GLM/GEE models included a dummy-coded (0/1) summary indicator for prenatal cocaine exposure, dummy-coded terms to index the assessment visits, and a term for the child's age at each visit. The raw total scores for the eight CPT indicators were used as dependent variables. These scores were first standardized by converting the sample mean for each assessment visit to zero, with an SD of 1, allowing the scores at each assessment visit to vary similarly along this continuum. This transformation allows the interpretation of the slope to be the same for each assessment, with each unit change in cocaine exposure reflected by "x" followed by "y" unit change in the attention measure.

RESULTS

Sample Demographics

Among the 476 full-term African-American infants in the Miami Prenatal Cocaine Study (MPCS) follow-up cohort, 415 children (196 non-cocaine-exposed, 219 cocaine-exposed) completed at least one continuous performance test (CPT) assessment at 5 and/or 7 years and are included in this report. As shown in Table 1, mothers in the cocaine-exposed group tended to be older, had less prenatal care, were less likely to be primigravida, and were more likely to be unemployed. Additionally, cocaine-exposed infants exhibited lower birth growth measures and gestational age relative to non-cocaine-exposed infants. The non-cocaine-exposed group also included a number of infants exposed to alcohol, tobacco, and/or marijuana. The two groups of comparison infants (i.e., those with alcohol, tobacco, and/or marijuana [ATM] but no cocaine exposure and those with no drug exposures) did not differ on any of the infant characteristics reported in Table 1 (data not shown). These groups were also similar in terms of maternal characteristics measured at birth with a few exceptions: the ATM mothers were a bit older, were less likely to be primigravida, and had fewer prenatal care visits ($p < .05$). Table 2 summarizes self-reported rates and median amounts of alcohol, tobacco, marijuana, and cocaine use during pregnancy. Mothers who used cocaine during pregnancy were more likely to report ATM use and reported a higher level of tobacco use. In the original cohort, 58%, 48%,

and 46% of the mothers used cocaine in the first, second, and third trimester, respectively. Approximately half of the sample used powder cocaine and half used crack cocaine.²⁷ The pattern of cocaine use for this subsample did not differ significantly from that of the original cohort.

Table 4 depicts selected social and demographic characteristics measured at each assessment. As indicated at one or both visits, caregivers of cocaine-exposed children were significantly less educated, were more often unemployed, and were more likely to self-admit past-year use of cocaine, tobacco, and marijuana. Also, cocaine-exposed children were less likely to be in the care of their biological mothers.

Table 5 summarizes mean CPT scores at 5 and 7 years. There were no group differences in mean ages at each assessment. Cohort retention based on examination attendance was 87%. At each visit, some of the children attended but did not complete the CPT task due to severe cognitive or behavioral difficulties (42 at 5 years and 14 at 7 years) or due to computer or coding problems (five at 5 years). A total of 368 and 401 children completed the CPT measure at 5 and 7 years, respectively, with 354 completing both assessments. There were 61 children for whom no CPT data were obtained. There were no statistically significant differences between cocaine-exposed and non-cocaine-exposed children with regard to CPT measure completion, examination attendance, or cognitive delays (in the overall sample or in the subsamples of measure completers and measure noncompleters). However, there was a statistically significant difference with regard to cognitive delay (i.e., IQ <70) between the children who completed the CPT measure and those who did not, with those who did not complete the measure typically having an IQ less than 70 at age 5 (11.4% of the Test of Variables of Attention (TOVA) completers vs 48.8% of the TOVA noncompleters; $p < .01$) and age 7 years (18.8% of the Conners' completers vs 55.6% of the Conners' noncompleters; $p < .01$). There were additional CPT noncompleters (six at 5 years and five at 7 years) who did not have IQ data available due to severe cognitive delay.

Multivariate Models

A series of longitudinal GLM/GEE models were conducted to evaluate variation in effect estimates summarizing the relationship between prenatal cocaine exposure and CPT indicators at 5 and 7 years, with consideration for a number of prenatal and postnatal factors. Model 1 (Table 6), which serves as baseline adjusted only for child's age at testing and gender, showed cocaine-associated increases in omission errors at both time points (at age 5, $p < .02$; at age 7, $p < .01$). The size of the observed between-group difference in omission error test performance was about 25% of the total sample SD at age 5 and about 28% of the total sample SD at age 7, with poorer performance (higher scores) in the cocaine-exposed group. There was no difference between the two slopes for omission errors at ages 5 and 7, suggesting that a single estimate served well to summarize the estimated impact of prenatal cocaine exposure on this facet of attention processing. The summary estimate, which borrows information across the age 5 and 7 omission test scores, was 0.27 (95% confidence interval [CI]: 0.11, 0.42; $p = .001$).

No between-group differences were found with respect to commission errors (at age 5 years, $p > .90$; at age 7 years, $p > .25$). Model 1 results revealed cocaine-associated increases in response time scores at age 7 years (i.e., slower reaction to the target; $p < .01$) but not age 5 years. Subsequent GLM/GEE modeling confirmed that two separate slope estimates, one for response time at 5 years and one at 7 years, were needed to summarize the data. Compared to non-cocaine-exposed, prenatally cocaine-exposed children also showed increased response time variance (i.e., greater inconsistency in responding) at age 7 ($p < .01$) but not age 5 years. Nevertheless, when the difference between these two slopes (i.e., response time variability at age 5 years and response time variability at age 7 years) was tested, data indicated that a single slope, borrowing information across ages 5 and 7 years, was sufficient for summarizing

prenatal cocaine's effect on variability of responses ($D = 0.26$; 95% CI: 0.11, 0.41; $p = .001$). All estimates remained stable with statistical adjustment for mother's age, educational level, marital status, and employment status at time of delivery; prenatal exposure to tobacco, alcohol, and marijuana; primigravida; and prenatal care visits (Table 6, model 2).

Next, model 2 was elaborated to assess statistical independence of the observed cocaine-associated deficits in relation to birth and postnatal characteristics that might be outcomes of prenatal cocaine exposure. These variables were not considered to be confounding variables because they are positioned temporally after cocaine exposure and some of them are known to be responsive to prenatal cocaine exposure. Terms for gestational age and birth growth (weight, length, and head circumference) were added to model 2 separately, whereupon estimates did not change appreciably (Table 6, models 3 and 4). The following postnatal factors measured at age 5 years were then introduced to model 2 one at a time (data not shown): biological mother as the primary caregiver (yes/ no); primary caregiver's reported past-year drug use (separate variables for alcohol, tobacco, marijuana, and cocaine), educational level, marital status, and employment; and child's placement in day care, past-year receipt of special developmental services; lead exposure levels ($\geq 10 \mu\text{g/dL}$) at 3 and/or 5 years, and IQ at age 5 years. In general, these postnatal variables were not associated with the outcomes of interest ($p \geq .20$), and the estimated slopes for cocaine-associated attention deficits did not change appreciably when the variables were included. Exceptions were child's IQ at age 5 years and postnatal caregiver marijuana smoking and employment status, all of which were related to CPT performance ($p < .20$). Studied in separate models, these covariate terms yielded a slight attenuation of the cocaine-associated deficit in omission scores at age 5 years, but no appreciable attenuation of slopes for other observed prenatal cocaine-associated deficits. Receipt of special developmental services was associated with CPT performance ($p < .001$), but inclusion of this term did not yield any appreciable change in the cocaine slope estimates.

DISCUSSION

The present report provides additional longitudinal evidence of sustained attention deficits in prenatally cocaine-exposed children. It extends previous work reported from the Miami Prenatal Cocaine Study (MPCS)²⁶ by examining the association between prenatal cocaine exposure and multiple indicators of attention processing measured by continuous performance tests (CPTs) administered at ages 5 and 7 years. Children exposed *in utero* to cocaine made more CPT omission errors at both age points. On average, the estimated magnitude of the cocaine-associated deficit, with varying levels of covariate control, was approximately 25% of an SD unit. No cocaine-associated increases in commission errors were evident at either age. Between-group differences were observed on response time and response time consistency at age 7 but not age 5 years. That is, at age 7 years, prenatally cocaine-exposed children responded more slowly to the stimuli and were more inconsistent in their responding than non-cocaine-exposed children. The estimated magnitude of the cocaine-associated deficit with varying levels of covariate control was approximately 30% and 31% of an SD unit for response time and response time consistency, respectively, at age 7 years. Importantly, these estimates remained highly stable with statistical adjustment for potential confounding influences, including other prenatal drug exposures.

The slower and more variable CPT responses observed in this study, when considered in combination with more omission errors, lends further support for a profile of impaired sustained attention among cocaine-exposed children relative to non-cocaine-exposed controls.³⁵ These results are consistent with previously published findings from the MPCS documenting an increase in omission errors as an indicator of sustained attention processing,²⁶ as well as reports from other investigations. Animal studies have found persistent impairments in sustained attention and the ability to maintain alertness to the task following gestational exposure to

cocaine,^{7,9} and clinical reports with school-age children have noted cocaine-associated increases in the number of CPT omission errors.^{23,42} In addition, Eghbalieh et al⁴³ reported greater response time and response variability in relation to prenatal cocaine/amphetamine exposure in a small group of 6- and 7-year olds, and, in another small study, Heffelfinger et al⁴⁴ reported slower response times on a visual attention task among cocaine-exposed children ages 14 to 60 months. Mayes et al,⁴⁵ however, found that cocaine-exposed children responded more quickly on a CPT relative to non-cocaine-exposed controls. Others have not found evidence of cocaine-associated difficulties in sustained attention on the CPT in childhood.²⁵

Differences in response time and variability between cocaine-exposed and non-cocaine-exposed children were evident at 7 but not 5 years of age. It is possible that this inconsistency was due to variations in the task parameters of the two different CPTs used at these time points. Alternatively, cocaine-related differences in response time and consistency indicators may have emerged with maturation. In general, the ability to sustain attention and inhibit irrelevant responses as measured by the CPT appears to develop considerably during childhood.^{34,46,47} Preliminary data suggest that children show significant gains in the ability to respond quickly and accurately on a CPT between the ages of 5 and 7 years⁴⁸ (Greenberg and Crosby, unpublished, 1992; available from Universal Attention Disorders, Los Alamitos, CA). Therefore, it may be that subtle cocaine-associated difficulties may become more apparent during the school-age years as attention-processing skills continue to develop.

Children with prenatal cocaine exposure in the current study did not exhibit the hypothesized increase in commission errors, an indicator of impulsivity or response inhibition. Richardson and colleagues also found greater omission errors in the absence of a commission effect among 6-year-old cocaine-exposed children.^{22,49} However, other studies suggest that children exposed *in utero* to cocaine have difficulty with impulsivity. For example, greater CPT commission errors have been reported for cocaine-exposed children,^{23–25} and cocaine exposure has been associated with poorer impulse control on delay tasks.^{18,19,50} A plausible explanation is that the CPT tasks in this study were not sufficiently challenging or stressful to elicit impulsive responding. Others²³ have reported more commission errors were made by cocaine- and other drug-exposed preschoolers relative to non-drug-exposed controls after distractors were added to a CPT task. Similarly, Savage et al.²⁵ only found cocaine-associated increases in commission errors on the Gordon Diagnostic System (GDS) Distractibility Task, the most difficult of the GDS tasks. This is consistent with the hypothesis that cocaine-exposed children have difficulty modulating arousal and tend to perform more poorly under stressful conditions and when highly aroused.⁴⁵ In addition, impulsivity is thought to be a broad construct encompassing a wide range of behaviors including speedy or careless decision-making, inability to delay reward, and failure to inhibit a motor response. Disinhibition as reflected in a greater number of CPT commission errors, likely captures only one aspect of impulsivity. Cocaine-exposed children in this sample may perform more poorly on measures tapping other components of impulsivity, such as delay of gratification and risk taking.

Although study results indicate greater attention problems in cocaine-exposed children compared to non-cocaine-exposed children, the clinical significance is as yet unclear (e.g., in terms of later school performance, which is currently under study as part of a preadolescent assessment). The CPT is just one measure of attention and response inhibition, and CPT results should be considered in the context of other clinical data including structured interviews and rating scales from multiple informants as well as behavioral observations in establishing the presence or absence of a clinically significant attention problem and a diagnosis of attention-deficit/hyperactivity disorder (ADHD). Moreover, the size of the cocaine effect across the CPT indicators in this study was small (i.e., 0.25–0.32 SDs) and the mean CPT standard scores for the cocaine-exposed group were generally within the normal range, suggesting overall subtle cocaine-associated deficits in sustained attention. It is important to note, nevertheless, that even

mild/moderate attention problems and subclinical ADHD symptoms may be associated with clinically meaningful impairments in academic, behavioral, and social functioning.^{51–53}

This study has numerous methodological strengths including prospective enrollment of cocaine-exposed infants and demographically similar controls and verification of prenatal drug exposure by bioassays. Also, the sample size is sufficiently large, with excellent retention of the original birth cohort. Use of advanced multivariate longitudinal modeling techniques, i.e., general linear model/generalized estimating equations (GLM/GEE),⁴⁰ allowed for the estimation of the prenatal cocaine-attention relationship while statistically adjusting for prenatal exposure to other drugs, as well as other potentially confounding influences, and while taking into account the interdependencies among the CPT indicators. Other advantages of the GLM/GEE modeling approach are that it makes use of all available data (i.e., does not exclude subjects with missing data) and does not require the strict distributional assumptions of repeated measures analysis of variance.

Nevertheless, certain study features and possible limitations should be considered in interpreting results. As with impulsivity, attention is multifaceted; however, attention functioning was measured in this study using only the CPT, which is known primarily as a measure of vigilance or sustained attention. Other components of attention such as focus/execute and shift were not evaluated. In addition, while the CPT provides an objective, standardized assessment of sustained attention, it is not without weakness. CPT performance does not strongly or consistently correlate with inattention and impulsivity as measured by parent and teacher report and direct behavioral observations in clinical samples,^{54–56} and its diagnostic utility has been questioned, particularly in distinguishing ADHD from other psychological disorders.^{57,58} Epstein et al⁵⁹ found that while CPT parameters were associated with ADHD symptomatology in general, there was little evidence of domain- or symptom-specific correspondence with CPT indicators. In our overall sample, CPT omission errors were related to the Attention Problems subscale from the parent-report Child Behavior Checklist, and CPT commission errors, response time, and response variability were associated with performance on the NEPSY Attention/Executive Function tasks, providing some evidence of convergent validity. CPT performance is potentially influenced by a variety of environmental and personal factors, including other cognitive processes such as phonological awareness and memory. In this study, the greater number of omission errors with slower and more variable responding was interpreted as inattention; however, a similar profile has been observed in children with memory problems and has been interpreted as inefficient allocation of processing resources rather than attention difficulties.⁶⁰

The majority of the mothers in the cocaine group also used varying amounts of tobacco, alcohol, and/or marijuana during pregnancy. Although these prenatal drug exposures were included as covariates in analytic models, such statistical control may not reveal potential additive and/or interactive effects among drugs and their impact on child neurodevelopment. Also, the current study used a dichotomous indicator of prenatal cocaine exposure across pregnancy. The issues of exposure severity and timing are not addressed here but may be important in delineating the degree of cocaine-associated impairments in sustained attention. The present cohort included African-American full-term infants, drawn from inner-city, low-income neighborhoods. These sampling restrictions promoted greater similarity between groups with respect to the biological, social, and environmental determinants of development, increasing statistical power and the ability to detect cocaine-related effects. However, as a result, the generalizability of study findings is limited to similar populations. Finally, as prenatal cocaine exposure has been linked with prematurity and congenital anomalies in some studies, the exclusion of infants with these conditions in this study may have resulted in an underestimation of cocaine-associated effects on attention and response inhibition.

In conclusion, study findings support the inference of prenatal cocaine-associated impairments in attention processing. Results suggest that such deficits are generally persistent across the years bridging the preschool and school-age period and appear to be specific to prenatal cocaine exposure when considering the influence of other prenatal substance exposures and confounding influences. As research has shown that the ability to sustain attention develops considerably during the primary school years,⁴⁶ it is essential that the relationship between prenatal cocaine and attention processing be assessed in these children as they age into adolescence, incorporating multiple measures that tap additional elements of attention.⁶¹ Also, it will be important to determine the “real-world” impact of such attention impairments, for example, whether these deficits are associated with a greater risk of diagnosis of attention and learning disorders and whether they negatively affect social and academic outcomes. Finally, maternal cocaine/polydrug use is associated with a number of other factors (e.g., poverty, violence exposure, psychological distress, poor parenting) that place children at risk of developmental difficulties. Future work should consider multiple determinants of attention functioning in cocaine-exposed children and explore additional social and environmental influences that may moderate or mediate outcomes.

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REFERENCES

1. Harvey JA. Cocaine effects on the developing brain: current status. *Neurosci Biobehav Rev* 2004;27:751–764. [PubMed: 15019425]
2. Mayes LC. Developing brain and in utero cocaine exposure: effects on neural ontogeny. *Dev Psychopathol* 1999;11:685–714. [PubMed: 10624721]
3. Brunzell DH, Ayres JJB, Meyer JS. Effects of prenatal cocaine exposure on latent inhibition in 1-year-old female rats. *Pharmacol Biochem Behav* 2002;72:795–802. [PubMed: 12062568]
4. He N, Bai J, Champoux M, et al. Neurobehavioral deficits in neonatal rhesus monkeys exposed to cocaine in utero. *Neurotoxicol Teratol* 2004;26:13–21. [PubMed: 15001210]
5. Garavan H, Morgan RE, Mactutus CF, et al. Prenatal cocaine exposure impairs selective attention: evidence from serial reversal and extradimensional shift tasks. *Behav Neurosci* 2000;114:725–738. [PubMed: 10959532]
6. Romano AG, Harvey JA. Prenatal exposure to cocaine disrupts discrimination learning in adult rabbits. *Pharmacol Biochem Behav* 1996;53:617–621. [PubMed: 8866963]
7. Morgan RE, Garavan HP, Mactutus CF, et al. Enduring effects of prenatal cocaine exposure on attention and reaction to errors. *Behav Neurosci* 2002;116:624–663. [PubMed: 12148929]
8. Kosofsky BE, Wilkins AS. A mouse model of transplacental cocaine exposure: clinical implications for exposed infants and children. *Ann N Y Acad Sci* 1998;846:248–261. [PubMed: 9668412]
9. Gendle MH, Strawderman MS, Mactutus CF, et al. Impaired sustained attention and altered reactivity to errors in an animal model of prenatal cocaine exposure. *Dev Brain Res* 2003;147:85–96. [PubMed: 14741754]
10. Gendle MH, White TL, Strawderman M, et al. Enduring effects of prenatal cocaine exposure on selective attention and reactivity to errors: evidence from an animal model. *Behav Neurosci* 2004;118:290–297. [PubMed: 15113253]
11. Overstreet DH, Moy SS, Lubin DA, et al. Enduring effects of prenatal cocaine administration on emotional behavior in rats. *Physiol Behav* 2000;70:149–156. [PubMed: 10978490]
12. Morrow CE, Bandstra ES, Anthony JC, et al. Influence of prenatal cocaine exposure on full-term infant neurobehavioral functioning. *Neurotoxicol Teratol* 2001;23:533–544. [PubMed: 11792523]
13. Richardson GA, Hamel SC, Goldschmidt L, et al. The effects of prenatal cocaine use on neonatal neurobehavioral status. *Neurotoxicol Teratol* 1996;18:519–528. [PubMed: 8888016]

14. Coles CD. Effects of cocaine and other drugs on the infant. *NIDA Res Monogr* 1992;119:121–125. [PubMed: 1435966]
15. Bard KA, Coles CD, Platzman KA, et al. The effects of prenatal drug exposure, term status, and caregiving on arousal and arousal modulation in 8-week-old infants. *Dev Psychobiol* 2000;36:194–212. [PubMed: 10737865]
16. Bendersky M, Lewis M. Arousal modulation in cocaine-exposed infants. *Dev Psychol* 1998;34:555–564. [PubMed: 9597364]
17. Mayes LC, Bornstein MH, Chawarska K, et al. Impaired regulation of arousal in 3-month-old infants exposed prenatally to cocaine and other drugs. *Dev Psychopathol* 1996;8:29–42.
18. Bendersky M, Lewis M. Prenatal cocaine exposure and impulse control at two years. *Ann N Y Acad Sci* 1998;846:365–367. [PubMed: 9668426]
19. Espy KA, Kaufmann P, Glisky M. Neuropsychologic function in toddlers exposed to cocaine in utero: a preliminary study. *Dev Neuropsychol* 1999;15:447–460.
20. Fried PA, Watkinson B. Differential effects on facets of attention in adolescents prenatally exposed to cigarettes and marihuana. *Neurotoxicol Teratol* 2001;23:421–430. [PubMed: 11711244]
21. Coles CD, Platzman KA, Lynch ME, et al. Auditory and visual sustained attention in adolescents prenatally exposed to alcohol. *Alcohol Clin Exp Res* 2002;26:263–271. [PubMed: 11964567]
22. Richardson GA, Conroy ML, Day NL. Prenatal cocaine exposure: effects on the development of school-age children. *Neurotoxicol Teratol* 1996;18:627–634. [PubMed: 8947939]
23. Dow-Edwards D, Mayes L, Spear L, et al. Cocaine and development: clinical, behavioral, and neurobiological perspectives—a symposium report. *Neurotoxicol Teratol* 1999;21:481–490. [PubMed: 10492383]
24. Noland JS, Singer LI, Short EJ, et al. Prenatal drug exposure and selective attention in preschoolers. *Neurotoxicol Teratol* 2005;27:429–438. [PubMed: 15939203]
25. Savage J, Brodsky NL, Malmud E, et al. Attentional functioning and impulse control in cocaine-exposed and control children at age ten years. *J Dev Behav Pediatr* 2005;26:42–47. [PubMed: 15718883]
26. Bandstra ES, Morrow CE, Anthony JC, et al. Longitudinal investigation of task persistence and sustained attention in children with prenatal cocaine exposure. *Neurotoxicol Teratol* 2001;23:545–559. [PubMed: 11792524]
27. Bandstra ES, Morrow CE, Anthony JC, et al. Intrauterine growth of full-term infants: impact of prenatal cocaine exposure. *Pediatrics* 2001;108:1309–1319. [PubMed: 11731653]
28. Schneiderman, JF. Nonmedical drug and chemical use in pregnancy. In: Koren, G., editor. *Maternal-Fetal Toxicology: A Clinician's Guide*. New York, NY: Marcel Dekker, Inc.; 1990. p. 301–320.
29. Mulé S, Casella GA. Confirmation and quantitation of cocaine, benzoylecgonine, ecgonine methyl ester in human urine by GC/MS. *J Anal Toxicol* 1988;12:153–155. [PubMed: 3386211]
30. Greenberg, L.; Leark, R.; Dupuy, T., et al. *Test of Variables of Attention (T.O.V.A. and T.O.V.A.-A.)*. Los Alamitos, CA: Universal Attention Disorders; 1996.
31. Rugino TA, Copley TC. Effects of modafinil in children with attention-deficit/hyperactivity disorder: an open-label study. *J Am Acad Child Adolesc Psychiatry* 2001;40:230–235. [PubMed: 11211372]
32. Corman, CL.; Greenberg, LM.; Crosby, R. The assessment of medication effects in Attention Deficit Disorder using the Test of Variables of Attention (T.O.V.A.). Presented at: 8th Annual Medicine Meets Virtual Reality Conference; January 27–30, 2000; Newport Beach, CA:
33. Forbes G. Clinical utility of the Test of Variables of Attention (TOVA) in the diagnosis of attention-deficit/hyperactivity disorder. *J Clin Psychol* 1998;54:461–476. [PubMed: 9623751]
34. Greenberg LM, Waldman ID. Developmental normative data on the test of variables of attention (T.O.V.A.). *J Child Psychol Psychiatry* 1993;34:1019–1030. [PubMed: 8408366]
35. Conners, CK. *Conners' Continuous Performance Test (CPT)*. Toronto, Canada: Multi-Health Systems; 1995.
36. Achenbach, TM. *Manual for the Child Behavior Checklist/4-18 & 1991 Profile*. Burlington, VT: University of Vermont, Department of Psychiatry; 1991.
37. Korkman, M.; Kirk, U.; Kemp, S. *NEPSY. A Developmental Neuropsychological Assessment Manual*. San Antonio, TX: Psychological Corporation; 1997.

38. Wechsler, D. Wechsler Individual Achievement Test (WIAT). San Antonio, TX: Psychological Corporation; 1993.
39. Wechsler, D. Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R). San Antonio, TX: Psychological Corporation; 1989.
40. Diggle, P.; Heagerty, P.; Liang, KY., et al. Analysis of Longitudinal Data. New York, NY: Oxford University Press; 2002.
41. Statacorp. Stata Statistical Software. College Station, TX: Stata Corporation; 2003.
42. Leech SL, Richardson GA, Goldschmidt L, et al. Prenatal substance exposure: effects on attention and impulsivity of 6-year-olds. *Neurotoxicol Teratol* 1999;21:109–118. [PubMed: 10192271]
43. Eghbalieh B, Crinella FM, Hunt LE, et al. Prenatal stimulant exposure effects of alerting and executive control in six- and seven-year-olds. *J Atten Disord* 2000;4:5–13.
44. Heffelfinger A, Craft S, Shyken J. Visual attention in children with prenatal cocaine exposure. *J Int Neuropsychol Soc* 1997;3:237–245. [PubMed: 9161102]
45. Mayes LC, Grillon C, Granger R, et al. Regulation of arousal and attention in preschool children exposed to cocaine prenatally. *Ann N Y Acad Sci* 1998;846:126–143. [PubMed: 9668402]
46. Conners CK, Epstein JN, Angold A, et al. Continuous performance test performance in a normative epidemiological sample. *J Abnorm Child Psychol* 2003;31:555–562. [PubMed: 14561062]
47. Lin CCH, Hsiao CK, Chen WJ. Development of sustained attention assessed using the continuous performance test among children 6–15 years of age. *J Abnorm Child Psychol* 1999;27:403–412. [PubMed: 10582841]
48. Turner, A.; Sandford, JA. A normative study of IVA: Integrated Visual and Auditory Continuous Performance Test. Presented at Annual Convention of the American Psychological Association; New York, NY: 1995.
49. Richardson GA. Prenatal cocaine exposure: a longitudinal study of development. *Ann N Y Acad Sci* 1998;846:144–152. [PubMed: 9668403]
50. Bendersky M, Gambini G, Lastella A, et al. Inhibitory motor control at five years as a function of prenatal cocaine exposure. *J Dev Behav Pediatr* 2003;24:345–351. [PubMed: 14578695]
51. Hudziak JJ, Heath AC, Madden PF, et al. Latent class and factor analysis of DSM-IV ADHD: a twin study of female adolescents. *J Am Acad Child Adolesc Psychiatry* 1998;37:848–857. [PubMed: 9695447]
52. Todd RD, Sitdhiraksa N, Reich W, et al. Discrimination of DSM-IV and latent class attention-deficit/hyperactivity disorder subtypes by educational and cognitive performance in a population-based sample of child and adolescent twins. *J Am Acad Child Adolesc Psychiatry* 2002;41:820–828. [PubMed: 12108807]
53. Costello EJ, Shugart MA. Above and below the threshold: severity of psychiatric symptoms and functional impairment in a pediatric sample. *Pediatrics* 1992;90:359–368. [PubMed: 1518689]
54. Naglieri JA, Goldstein S, Delauder BY, et al. Relationships between the WISC-III and the Cognitive Assessment System with Conners' rating scales and continuous performance tests. *Arch Clin Neuropsychol* 2005;20:385–401. [PubMed: 15797174]
55. McGee RA, Clark SE, Symons DK. Does the Conners' Continuous Performance Test aid in ADHD diagnosis? *J Abnorm Child Psychol* 2000;28:415–424. [PubMed: 11100916]
56. Barkley RA. The ecological validity of laboratory and analogue assessment methods of ADHD symptoms. *J Abnorm Child Psychol* 1991;19:149–178. [PubMed: 2056161]
57. Riccio CA, Waldrop JJM, Reynolds CR, et al. Effects of stimulants on the continuous performance test (CPT): implications for CPT use and interpretation. *J Neuropsychiatry Clin Neurosci* 2001;13:326–335. [PubMed: 11514638]
58. Nichols SL, Waschbusch DA. A review of the validity of laboratory cognitive tasks used to assess symptoms of ADHD. *Child Psychiatry Hum Dev* 2004;34:297–315. [PubMed: 15039603]
59. Epstein JN, Erkanli A, Conners CK, et al. Relations between continuous performance test performance measures and ADHD behaviors. *J Abnorm Child Psychol* 2003;31:543–554. [PubMed: 14561061]
60. Eliason MJ, Richman LC. The Continuous Performance-Test in learning-disabled and nondisabled children. *J Learn Disabil* 1987;20:614–619. [PubMed: 3694041]

61. Mirsky AF, Anthony BJ, Duncan CC, et al. Analysis of the elements of attention: a neuropsychological approach. *Neuropsychol Rev* 1991;2:109–145. [PubMed: 1844706]

Table 1

Maternal and Infant Characteristics at Birth Enrollment (n = 415)

	Non-Cocaine-Exposed (n = 196)	Cocaine-Exposed (n = 219)
Maternal characteristics		
Maternal age, yr ^a	23.8(5.4)	28.9(4.9)
Education, yr	11.3(1.4)	11.1(1.4)
Unemployed, % ^a	83	95
Never married, %	88	91
Primigravida, % ^a	24	6
Prenatal care ≥4 visits, % ^a	84	69
Infant characteristics		
Birth weight, g ^a	3305(508)	2977(475)
Birth length, cm ^a	50.8(2.3)	48.9(2.5)
Birth head circumference, cm ^a	33.8(1.5)	33.1(1.5)
Gestational age, wk ^a	39.7(1.4)	39.4(1.3)
Male, %	50	49.8

Numbers represent means (SD) or percentages where indicated.

^a $p < .01$.

Table 2**Maternal Self-Reported Alcohol, Tobacco, Marijuana, and Cocaine Use During Pregnancy**

Substance	Non-Cocaine-Exposed (n = 196)		Cocaine-Exposed (n = 219)	
	Median (Min, Max) ^a	% (No.)	Median (Min, Max) ^a	% (No.)
Alcohol (no. of drinks) ^c	54 (2,1680)	30.6 (60)	97 (1,5226)	67.1 (147)
Tobacco (no. of cigarettes) ^{b,c}	1008 (21,5880)	15.8 (31)	2282 (1,8820)	75.8 (166)
Marijuana (no. of joints) ^c	37 (1,807)	12.2 (24)	24 (1,1229)	43.8 (96)
Cocaine/crack (no. of lines/rocks)			135 (1,19320)	69.4 (152)

^aMedian values based only on mothers reporting use, calculated using total exposure composites: (number of weeks used) × (usual number of days per week) × (usual dose per day).

^b $p < .05$, between-group comparisons of median maternal drug use (columns 1 and 3).

^c $p < .01$, between-group comparisons of percentage of maternal drug use (columns 2 and 4).

Table 3
Continuous Performance Test Variables Measured in the Study

Continuous Performance Test Measures		Description
TOVA at 5 Yr	Conners' at 7 Yr	
No. of omission errors	No. of omission errors	The number of targets to which the child did not respond. This is interpreted as a measure of inattention.
No. of commission errors	No. of commission errors	The number of times the child responded to a nontarget. This is interpreted as a measure of impulsivity.
Mean correct response time	Hit response time	The mean response time (in milliseconds) for all target responses over the entire testing session. This is interpreted as a measure of processing and response time.
SD of response times	Variability of SEs	The consistency of response times. This is interpreted as a measure of variability or consistency in performance.

TOVA, Test of Variables of Attention.

Table 4
Caregiver and Child Characteristics Assessed at the 5- and 7-Year Assessment Visits

	Non-Cocaine-Exposed		Cocaine-Exposed	
	n		n	
Biological mother as caregiver, %				
5 yr ^a	189	95.8	206	67.5
7 yr ^a	194	95.9	205	59.0
Caregiver's education, yr				
5 yr	187	11.5(1.5)	202	11.2(1.8)
7 yr ^b	194	11.7(1.5)	204	11.3(2.0)
Caregiver unemployment, %				
5 yr	187	59.9	202	64.4
7 yr ^a	194	28.4	203	57.6
Caregiver past year cocaine use, %				
5 yr ^a	186	2.7	201	21.4
7 yr ^a	194	3.1	204	19.6
Caregiver past year marijuana use, %				
5 yr ^b	186	16.7	201	26.9
7 yr	194	15.5	204	17.7
Caregiver past year alcohol use, %				
5 yr	186	64.5	199	60.3
7 yr	194	57.7	204	55.4
Caregiver past year tobacco use, %				
5 yr ^a	186	22.6	200	56.5
7 yr ^a	194	24.2	204	54.4
Child receipt of special services, %				
5 yr	186	11.3	198	13.6
7 yr	191	29.3	204	28.9
Child receipt of day care, %				
5 yr	186	20.4	202	26.7
Child blood lead level ≥ 10 $\mu\text{g/dL}$, %				
3 and/or 5 yr	192	8.3	217	14.3
Child intellectual functioning				
5 yr	188	82.3(11.0)	212	81.2(10.5)

Group n's for postnatal variables are drawn from the 415 subjects with available 5-year Test of Variables of Attention (n = 368) and/or 7-year Conners' Continuous Performance Test (n = 401) scores and the associated available data. Numbers represent mean (SD) or percentage where indicated.

^a $p < .01$.

^b $p < .05$.

Table 5
Test of Variables of Attention and Conners' Continuous Performance Test Scores at 5 and 7 Years, Respectively

TOVA	Raw Score				Standard Score ^a			
	Non-Cocaine-Exposed (n = 171)		Cocaine-Exposed (n = 197)		Non-Cocaine-Exposed (n = 171)		Cocaine-Exposed (n = 197)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Omission errors	31.7	27.1	38.5	29.3	87.3	22.2	80.9	22.8
Commission errors	19.5	14.6	20.1	15.6	91.6	18.3	91.8	19.4
Response time	699	136	707	135	93.9	21.6	90.7	20.8
Response time variability	261	67	277	73	98.0	18.4	93.3	19.2

Conners' CPT	Raw Score				Standard Score ^b			
	Non-Cocaine-Exposed (n = 194)		Cocaine-Exposed (n = 207)		Non-Cocaine-Exposed (n = 194)		Cocaine-Exposed (n = 207)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Omission errors	22.6	20.1	27.9	24.2	—	—	—	—
Commission errors	20.0	6.9	19.4	7.5	44.3	10.2	43.1	11.2
Hit reaction time	489	97	520	124	48.2	12.8	44.7	13.5
Variability of SEs	25.2	17.0	31.5	23.3	49.0	11.3	52.7	11.3

TOVA, Test of Variables of Attention; CPT, Continuous Performance Test.

^aTOVA standard scores have a mean of 100 and an SD of 15.

^bConners' CPT standard scores expressed as T scores, with a mean of 50 and an SD of 10. T scores are not available for omission errors.

Table 6

Estimated Attention Processing Differences Between Cocaine-Exposed and Non-Cocaine-Exposed Children at Ages 5 and 7 Years

Model	Attention Measure	Estimated Difference	95% CI	p Value
1	5-Yr omission errors	0.25	0.04,0.45	.019
	7-Yr omission errors	0.28	0.08,0.48	.005
	5-Yr commission errors	-0.004	-0.20,0.19	.968
	7-Yr commission errors	-0.11	-0.31,0.09	.269
	5-Yr response time	0.06	-0.16,0.27	.607
	7-Yr response time	0.31	0.11,0.51	.002
	5-Yr variability of responses	0.20	-0.01,0.40	.057
	7-Yr variability of responses	0.32	0.12,0.51	.002
2	5-Yr omission errors	0.24	0.01,0.47	.043
	7-Yr omission errors	0.27	0.05,0.50	.018
	5-Yr commission errors	-0.01	-0.24,0.22	.908
	7-Yr commission errors	-0.12	-0.34,0.10	.279
	5-Yr response time	0.05	-0.19,0.28	.704
	7-Yr response time	0.30	0.08,0.52	.008
	5-Yr variability of responses	0.19	-0.04,0.42	.110
	7-Yr variability of responses	0.31	0.07,0.54	.009
3	5-Yr omission errors	0.25	0.02,0.48	.035
	7-Yr omission errors	0.28	0.06,0.51	.014
	5-Yr commission errors	-0.001	-0.23,0.22	.991
	7-Yr commission errors	-0.11	-0.33,0.11	.338
	5-Yr response time	0.06	-0.18,0.30	.633
	7-Yr response time	0.31	0.09,0.53	.005
	5-Yr variability of responses	0.20	-0.03,0.43	.083
	7-Yr variability of responses	0.32	0.09,0.55	.007
4	5-Yr omission errors	0.24	0.01,0.48	.038
	7-Yr omission errors	0.28	0.05,0.50	.015
	5-Yr commission errors	-0.01	-0.24,0.22	.952
	7-Yr commission errors	-0.11	-0.33,0.10	.305
	5-Yr response time	0.05	-0.18,0.29	.665
	7-Yr response time	0.31	0.08,0.53	.007
	5-Yr variability of responses	0.19	-0.04,0.43	.099
	7-Yr variability of responses	0.31	0.08,0.54	.008

CI, confidence interval. Model 1 is the baseline model with adjustment for child gender and age at testing. Model 2 includes adjustment for child gender and age; mother's age, educational level, marital status, and employment status at time of delivery; prenatal exposure to tobacco, alcohol, and marijuana; primigravida; prenatal care visits. Model 3 includes Model 2 plus birth weight, birth length, and birth head circumference. Model 4 includes Model 2 plus gestational age.