THE EFFECTS OF PRENATAL COCAINE EXPOSURE ON ATTENTION AND READING: A LONGITUDINAL STUDY

By

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This dissertation is dedicated to the memory of my father, James V. Duckworth, Jr., who taught me to always “dream big" and to my mother, Mary A. Duckworth, who always encouraged to tackle any task that I thought I was "big enough" to handle.

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Animal studies and knowledge about the pharmacology of cocaine strongly suggest that maternal cocaine use during pregnancy has negative consequences for fetal development. However, significant neurobehavioral differences between infants and children with prenatal cocaine exposure (PCE) and well-matched comparison groups have not been found consistently. Attention is one area in which group differences have been reported, but the functional implications of these findings for reading or other school-related abilities remain uncertain.

A group of prospectively enrolled children who were prenatally exposed to cocaine, alcohol, tobacco, and marijuana (n = 120) were compared to a matched group of children who were exposed to alcohol, tobacco, and marijuana but not cocaine (n = 120). Both groups were predominantly poor and African American and did not differ by sex.

Significant group differences were higher levels of prenatal drug exposure, higher prenatal risk scores, shorter gestational ages, and smaller head circumferences at birth for the children with PCE.

Results indicated that neonatal attention as measured by three scales of the Brazelton Neonatal Behavioral Assessment Scale was not significantly associated with attentional measures administered at ages 5 and 7, including a continuous performance test, short term auditory attention (Digit Span), or three tasks involving visual scanning and visuomotor coordination (Letter Cancellation, Trail Making Test Part A, and the Coding subtest of the Wechsler Intelligence Scale for Children-III). Analyses also revealed that children with PCE did not perform significantly worse than non-exposed children on attention measures at ages 5 or 7 or on the Wechsler Individual Achievement Test reading subtests at age 7.

Structural equation modeling, however, demonstrated that PCE had an indirect effect on reading ability at age 7 that was mediated by head circumference at birth. The effect of PCE on birth head circumference was similar to that of prenatal exposure to alcohol or marijuana. Birth head circumference affected age 5 verbal ability which, in turn, was related to age 7 verbal ability and visual attention which, in turn, affected age 7 reading ability. The final model accounted for 68% of the variance in age 7 reading ability for the combined sample.

CHAPTER 1
INTRODUCTION

Overview of Attention

This manuscript begins with a brief review of definitions and models of attention, the neuroanatomical correlates of attention, attentional development over the course of infancy and early childhood, and measurement issues related to attention. In attempting to define attention, many writers begin with William James' now-famous observation that

> Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem to be several simultaneously possible objects or trains of thought. Focalization, concentration, and consciousness are of its essence. (James, 1890, pp. 381-382)

Enns (1990) has observed that many definitions of attention share a component of selectivity—that a primary function of attention is to select information for further processing. Similarly, Cohen (1993) argues that attention serves as a gatekeeper in facilitating "the selection of salient information and the allocation of cognitive processing appropriate to that information" much like the aperture and lens system of a camera (Cohen, 1993, p. 3). It is generally agreed that attention is not a unitary process, but a multifactorial process, involving a diverse set of behavioral phenomena

Based on this general understanding of attention, several researchers have attempted to construct models of the various components of attention. An empirically validated model of attention that integrates research from cognitive psychology and neuropsychology has been articulated by Mirsky, Anthony, Duncan, Ahearn and Kellam (1991). Mirsky et al. (1991) identified three "elements" of attention—focus, sustain, and

shift. The focus element involves selecting information for enhanced processing, which has been equated with attention itself. The focus element also includes an "execute" component, in which motor programs associated with focusing attention are activated. The sustain component is synonymous with vigilance or the ability to maintain focus and alertness over time. The third element, shift, represents the ability to change attentive focus in a flexible and adaptive manner.

Neuroanatomically, the three elements of attention in the Mirsky et al. model can be localized to various areas of the brain based on lesion studies of brain-impaired patients, animal lesion studies, and neuroimaging data (Mirsky et al., 1991). The focus-execute element is associated with the inferior parietal and superior temporal cortex and striatum of the basal ganglia. The parietal area is the primary cerebral locus of the focus-execute aspect of attention based on studies of adult neglect patients (Heilman, Watson, & Valenstein, 1993) as well as the connectivity of the parietal lobe with sensory, motor, limbic, thalamic and brain stem regions of the brain. It is worth noting, however, that unlike adults, children rarely show the full adult neglect syndrome even with parietal lesions (Ferro, Martins, & Tavora, 1984). The proposed role of superior temporal sulcus in focused attention in Mirsky's model is supported by studies of the architecture and connectivity of this area as well as studies of epilepsy patients who have undergone anterior temporal lobectomy although there are some conflicting data on this latter point (Mirsky et al., 1991). Inclusion of striatum in the anatomy underlying focused attention is based on its modulatory role in motor systems and the role of the caudate in delayed alternation and delayed response tasks (Mirsky et al., 1991).

The sustain element of attention is subserved by rostral midbrain structures, including the mesopontine reticular formation and midline and reticular thalamic nuclei. Regulation of arousal and maintenance of consciousness are the primary functions of the brain stem structures. Single unit recording studies in monkeys trained on a go/no-go visual attention task showed increased firing of Type II cells in the midline thalamus, superior colliculus, tectum, pons, and mesencephalic brain stem, suggesting a role in maintaining attention. In addition, studies involving stimulation of reticular nucleus of the thalamus have demonstrated that this thalamic nucleus modifies the influence of reticular formation effects on visual signals, specifically one's "readiness to respond" to visual stimuli in discrimination paradigms.

Neuroanatomically, the shift component of attention in Mirsky's model is the responsibility of the prefrontal cortex and also perhaps the medial frontal cortex and anterior cingulate gyrus (Mirsky et al., 1991). The role of the prefrontal cortex role in shifting attention is supported by studies of poor performance on the Wisconsin Card Sorting Test (WCST) by epilepsy patients who have undergone resection of the dorsolateral prefrontal cortex. Additional evidence comes from individuals with schizophrenia who show impaired performance on the WCST and reduced activation of the prefrontal areas in imaging studies. Preliminary inclusion of the medial frontal cortex and anterior cingulate gyrus in attentional shift is based on the firing patterns of Type II cells in these regions in monkeys during go/no-go visual discrimination tasks that are thought to measure both shifting attention as well as sustained attention, as discussed earlier (Mirksy et al., 1991).

Additional evidence supporting Mirksy's model of the neural substrates underlying different aspects of attention comes from neuroimaging studies of individuals with Attention Deficit/Hyperactivity Disorder (ADHD) and schizophrenia, two clinical disorders with significant attentional dysfunction. ADHD is a behavioral disorder characterized by hyperactivity, impulsivity, and inattentiveness. In a recent review of structural and functional neuroimaging studies of children and adolescents with ADHD, Hale, Hariri, and McCracken (2000) concluded that three sets of findings are emerging with some consistency: 1) reduced prefrontal and caudate volumes, 2) hypoperfusion and hypometabolism in prefrontal and striatal regions, and 3) lower levels of activation in the anterior cingulate during tasks involving stimulus selection and/or response inhibition. That the frontal areas involved in shifting attention and the striatal areas involved in sustained attention have been implicated in ADHD provides some support for Mirsky's model of attention.

Functional neuroimaging studies on the attentional deficits found in those with schizophrenia are another source of support for the neuroanatomical outline for Mirsky's model of attention. In Taylor's (1996) review of 24 functional neuroimaging studies using adults, almost half of the studies (11) found that patients with schizophrenia failed to show task-related increases in blood flow in the prefrontal area, using the WCST and similar paradigms. Studies of children and adolescents with childhood-onset schizophrenia also show reduction of frontal metabolism (Hendren, DeBacker, & Pandina, 2000). Thus, the neural mechanisms that may underlie the attentional deficits in schizophrenia for adults appear to be same for children and adolescents. Again, both sets of findings support Mirsky's localization of shifting attention to the prefrontal area.

One serious limitation of Mirsky's model is its underspecification of the role of neurotransmitter systems in attention. In contrast, Posner and Petersen's (1990) model of attention places strong emphasis on norepinephrine (NE) arising from the locus ceruleus in the rostral brain stem and extending to the posterior attention system, particularly in the right hemisphere. Norepinephrine is thought to play a crucial role in maintaining an alert state based on animal studies and the effects that drugs that manipulate NE levels have on the ability to shift attention (Posner & Petersen, 1990). Posner and Petersen's model is consistent with current theories that suggest that the core deficits in ADHD are in executive functions that regulate arousal, attention, and inhibition and that these deficits may be related etiologically to abnormalities in dopaminergic and noradrenergic pathways from the brainstem that serve to regulate cortico-striato-thalamo-cortical networks (Hale, Hariri, & McCracken, 2000). It should be noted, however, that pathways involving dopamine and norepinephrine are found throughout the brain, and this may be the reason that Mirsky and his colleagues have not included neurotransmitter components in their model of the neuroanatomical substrates of attention.

Despite this major limitation, the model of attention offered by Mirsky and colleagues has been confirmed empirically using principal components analysis in an epidemiological sample of elementary school children ($N = 435$) and in a sample of normal and neuropsychiatrically impaired adults ($N = 203$). Importantly, the focus-execute, sustain, and shift factors (in addition to an encode factor) were found in both samples, suggesting that attention operates according to similar processes in both children and adults. In both samples, the focus-execute factor was identified by significant loadings from the Digit Symbol Substitution subtest of the Wechsler Adult Intelligence

Scale-Revised (WAIS-R, Wechsler, 1981) or Coding subtest from the Wechsler Intelligence Scale for Children-Revised (WISC-R, Wechsler, 1980) and the Talland Letter Cancellation Test (Talland, 1965). The sustain factor was identified by significant loadings from a continuous performance test (CPT), specifically mean number of hits and mean reaction time. Finally, the shift factor was identified by the Wisconsin Card Sorting Test (Grant & Berg, 1993) percentage correct and number of categories achieved. The adult sample was also administered the Trail Making Test (Reitan & Wolfson, 1985), which had significant primary loadings on the focus-execute factor as well as significant secondary loadings on the sustain factor (Mirsky et al., 1991).

Overall, Mirsky's three factor model of attention, which has been confirmed empirically and has at least partially-specified neuroanatomical substrates for each factor, provides a solid foundation for studying attention in both children and adults.

Development of Visual Attention in Infants and Children

This review of the development of attention from the neonatal period through early to middle childhood will focus on studies of visual attention. Prior to reviewing the two major conclusions that can be drawn from the developmental literature on attention, a brief review of the measurement of attention in infants is warranted. Infant attention is generally studied using paradigms that rely on the visual modality and is measured clinically using motor orienting responses such as head turning and attempts at visual fixation to a stimulus. In the laboratory setting, psychophysiological measures, such as changes in heart rate and evoked brain potentials, have proven to be useful tools in measuring attention in newborns and young infants who have poor motoric control (Graham, 1992). Visual fixation on a stimulus, habituation to the stimulus in the form of

decreasing fixation times after continuous or repeated presentations, and reorientation to a novel stimulus are also common measures.

Generally, two major conclusions can be made from the literature on the development of visual attention in children: children's attentional capacities improve with age (Cooley & Morris, 1990) and some continuity exists between attentional abilities measured at infancy and those measured at later ages (Colombo, 1993; Enns, 1990). Based on their review of the experimental literature, Cooley and Morris (1990) suggest that the improvement in children's attentional abilities over time can be explained using two different theoretical frameworks. The first is an information processing framework that states that the limited attentional capacity of younger children increases as internal processing mechanisms develop with age. In the case of selective attention, the filtering mechanism of attention becomes more efficient and larger proportions of attentional resources can be allocated and allocated more flexibly to relevant rather than irrelevant aspects of a task. Similarly, in the case of sustained attention, a limited capacity model would predict that more effort is required of younger subjects than older subjects in order to perform well (Cooley & Morris, 1990).

The second theoretical framework used to explain children's improved attentional abilities over time is an ecological or perceptual learning framework. According to this framework, children learn with age to become more specific, systematic, economical, and task-directed in their perception and exploration. In doing so, children become better able to differentiate relevant from irrelevant information needed for a task. Thus, the perceptual learning framework tends to emphasize improvements over time in the quality of children's selective attention abilities (Cooley & Morris, 1990).

Generally, the literature suggests that children begin to develop control over their visual attentional resources between 7 and 13 years of age, but the development of efficient use of strategic methods for allocating attention continues through adulthood. Kaye and Ruskin (1990) conducted a series of three studies to investigate the relative roles of increased information capacity processing versus strategic allocation of attentional resources in children's improved performance on various attentional measures. Using a paradigm requiring shifting attention to a peripheral visual cue, the researchers found that age differences among 3rd graders, 6th graders and college students were only found for general alertness, a non-strategic capacity-related factor. In a divided attention task using two stimulus probability conditions, it was found that both younger and older children demonstrated adult-like strategic processing, but there were age differences in their efficient use of these strategies. The third study used a classification task and children at three different age levels ranging from 5 to 12 years. No qualitative differences in strategy use were found; however, quantitative differences in search rates were found, which in turn affected classification. Based on these three studies, the authors concluded that while adult-like strategies emerge early in childhood, their optimal use in complex tasks is dependent on the increased information processing efficiency that comes with age (Kaye & Ruskin, 1990).

The question of continuity in mental abilities generally, and attention in particular, has been studied in longitudinal samples. The two major paradigms used in these studies are habituation and response to novelty. Habituation is measured as either the rate of decline in looking behavior over repeated presentations of a stimulus or the fixation duration. Response to novelty is measured either by looking behavior to a new

stimulus simultaneously paired with an already-familiar stimulus (novelty preference) or as recovery of fixation to a new stimulus after habituation (recovery). Bornstein (1990) reviewed eight longitudinal studies that examined the predictive validity of habituation paradigms administered during the first six months of life for later cognitive performance. The median predictive correlation of habituation paradigms using different sensory modalities was .49, with a range from .28 to .63. Three-quarters of these studies focused on predicting IQ, two used language measures and one used the Bayley Scales of Infant Development (Bayley, 1969). Notably, these studies of infant attention used both normal and at-risk infant samples with the age at the second assessment ranging from 2 years to 8.5 years. A similar review by Colombo (1993) of 13 studies that specifically used fixation duration to predict a variety of outcome measures found correlations ranging from .29 to .77.

Colombo (1993) has also reviewed longitudinal studies of predictive validity of response to novelty measured in the first year of life with later cognitive measures. Based on the four studies that used recovery after habituation as their measure of response to novelty, few conclusions can be drawn, in part because recovery measures have poor reliability and stability (Colombo, 1993). In contrast, the predictive validity of novelty preference measures with later intellectual and cognitive function is more robust. The overall median correlation, based on 14 studies of novelty preference, is .47, with a range from .25 to .66; when only standardized IQ scores are used as the outcome measure, the median correlation increases slightly to .49 (Colombo, 1993). The majority of these studies used three IQ outcome measures: the Stanford-Binet (Thorndike, Hagen, & Sattler, 1986), the age-appropriate Weschler scale, or the Peabody Picture Vocabulary

Test-Revised (Dunn, Dunn, Robertson, & Eisenberg, 1981). Four studies used the Bayley Scales of Infant Development (Bayley, 1969), four used measures of language development and two examined memory. The age at first assessment ranged from 3 to 9 months, while the age at second assessment ranged from 1 to 7 years of age (Colombo, 1993). Overall, the reviews by Bornstein (1990) and Colombo (1993) suggest a moderate degree of predictive validity between experimental measures of attention and standardized cognitive assessments in early to middle childhood.

A handful of longitudinal studies have begun to examine the development of particular aspects of attention over time and how these components relate to other cognitive functions. In pre-term infants it has been found that fixation duration measured at 40 weeks conceptual age was predictive of performance on a focused attention task but not a sustained attention task administered at age 12 (Sigman, Cohen, Beckwith, Asarnow, & Parmelee, 1991). Notably, the focused attention measure was a signal detection task that also required speeded information processing. The correlations between the infant attentional measures and later attentional measures were -.36 and -.32, for the less difficult and more difficult version of the task, respectively. To explain their findings, the authors argue that both infant attention measures and childhood cognitive assessment may tap the efficiency of information processing. If this is the case, then an individual's relative capacity to process information efficiently would be expected to be stable from infancy to childhood. Furthermore, infant information processing abilities would not be expected to be associated with other measures of childhood attentional ability such as sustained attention (Sigman et al., 1991).

In another longitudinal cohort, Rose and Feldman (1995) found that an indirect measure of sustained attention (exposure time to meet criterion during a visual recognition memory task) acquired at 7 months of age in a sample of pre-term and full-term infants was significantly correlated with perceptual speed at 11 years of age. When IQ was partialed out, the correlations between the infant sustained attention measure and the perceptual speed measures were .33 for a visual matching task, .34 for a visual search task and .38 for the two measures combined (Rose & Feldman, 1995).

The significant correlations between sustained attention and perceptual speed in the Rose and Feldman (1995) study seem to support increased capacity and increased efficiency theories posited by information processing accounts. The authors also suggest, however, a second possible explanation for the significant correlation between sustained attention and perceptual speed: that the speed with which the child is able to respond is a function of his or her ability to filter out stimuli irrelevant to the task (Rose & Feldman, 1995). In this way, the sustained attention measure is also a measure of appropriately focused attention. Unfortunately, the researchers did not include any attentional assessments in their longitudinal battery so the relationship between the infant attentional measure cannot be compared to later childhood attentional measures.

One major limitation of the experimental literature on the development of children's attention, as with the models of attention reviewed earlier, is its neglect of the development of underlying brain systems. While neuropsychological studies of childhood attention, which tend to focus on deficits found in clinical populations, stress the importance of the developing neural substrates, they rarely elucidate specific brain-behavior relationships. More important perhaps is the fact that few studies in the

developmental neuropsychology literature have attempted to relate children's development of various components of attention—e.g., focus, shift, and sustain—to brain maturation (Cooley & Morris, 1990).

Measurement of Visual Attention in Infants and Children

As briefly reviewed in the previous section, a number of different experimental paradigms exist for measuring visual attention in infants. The number of clinical measures available for assessing attention in the first few years of life is not as plentiful. As a result, few developmental studies are available that explore the growth and change of attention using clinical measures. Arguably, the most commonly used assessment instrument for the study of infant attention is the Brazelton Neonatal Behavioral Assessment Scale (BNBAS). First developed in 1973, the BNBAS is designed to assess the newborn's adaptive responses to his or her new extrauterine environment and has been used for over 25 years in hundreds of research and clinical setting across the world (Nugent & Brazelton, 2000). Theoretically, development of the BNBAS is based on the assumption that early human development proceeds from a state of relative undifferentiation to one of increasing differentiation, articulation and hierarchic integration. More specifically, there are hypothesized four primary developmental tasks of the newborn, arranged hierarchically and related to increasing self-regulation. The first developmental task is organization of autonomic or physiological behavior, which involves homeostatic adjustment of the central nervous system including respiration, the startle response, tremors and temperature regulation. The second development task is control and regulation of motor behavior, including inhibition of random motor responses, development of better muscle tone and reduction of excessive motor activity. Third, the neonate must develop state regulation, the ability to modulate states of

consciousness including sleep, and deal with stress using strategies such as hand-to-mouth movements, communicating with the caregiver through crying and being consoled with the aid of the caregiver. The fourth and final task for the infant is regulation of affective interactive or social behavior, which involves maintaining prolonged alert periods, attending to visual and auditory stimuli within one's range and seeking out and engaging in social interaction with the caregiver (Nugent & Brazelton, 2000).

The development of the first three self-regulatory capacities can be seen as laying the foundation for the fourth, which is the rudimentary development of attention to external stimuli. Following regulation of internal stimuli, the neonate can turn to maintaining alertness or arousal, which is a prerequisite for directing, focusing and sustaining attention. With repeated assessments, the BNBAS describe this emerging process during the first couple of months of the newborn's life in the extrauterine environment. A more detailed description of the scale and its properties is found in the Methods chapter.

After the neonatal period, standardized measurements of infant attention are more difficult to come by. This is due, in part, to a variety of methodological challenges associated with developmental research, not the least of which is the problem of measurement equivalence (Hartmann & George, 1999). Measurement equivalence refers to the question of whether an assessment instrument measures the same construct at various developmental ages. For example, an "intelligence" test may be more a measure of verbal comprehension than reasoning at age 3 as compared to age 10. In addition, children's rapid changes in physical and behavioral maturation and experience can make transient performance levels difficult to capture (Hartmann & George, 1999). A variety of

design and data analytic techniques can be used to help guard against and test for measurement equivalence, but it is a thorny issue ever-present in developmental research and very difficult to overcome in infancy and childhood investigations.

Prenatal Cocaine Exposure and Attention

With the alarming rise in the use of cocaine by pregnant women since the mid-1980s, children who have been prenatally exposed to cocaine have emerged as a new clinical population in which to study the development of attention. That prenatal cocaine exposure has a teratogenic effect on development has generally been established. Cocaine has the potential to exert deleterious effects in variety of direct and indirect ways. Cocaine easily crosses both the placenta and the blood-brain barrier (Mayes, 1994). Most of what is known about the pharmacologic and other effects of cocaine on prenatal development has been learned through research on a variety of animal populations, including rats, mice, rabbits, and monkeys (Kosofsky & Wilkins, 1998; Lidow, 1998; Spear, 1995). There is a general consensus that animal models (despite differences in route of administration and other methodological problems) are useful analogues of prenatal cocaine exposure in humans (Needlman, Frank, Augustyn & Zuckerman, 1995). Three well-studied pharmacological effects of cocaine will be reviewed here. First, cocaine inhibits the reuptake of dopamine, serotonin and norepinephrine, thereby potentiating their actions (Akbari, Kramer, Whitaker-Azmitia, Spear & Azmitia, 1992; Dow-Edwards, 1995; Factor, Hart & Jonakait, 1993; Friedman & Wang, 1998; Leslie, Robertson, Jung, Libermann & Bennett, 1994; Mayes, 1994; Mactutus, Herman, & Booze, 1994; Ronnekliev, Fang, Choi & Chai, 1998; Vorhees, 1995). Second, cocaine causes vasconstriction and can reduce blood supply and oxygenation to a developing fetus, resulting in chronic or intermittent hypoxia (Dow-Edwards, 1995; Woods, 1996).

Third, cocaine acts as a potent local anesthetic, blocking sodium channels, thereby attenuating action potentials in excitable cells (Dow-Edwards, 1995).

In addition to its pharmacological effects, maternal use of cocaine can cause hypertension, placental aburption, spontaneous abortion, poor pregnancy weight gain and undernutrition secondary to appetite loss (Church, Crossland, Holmes, Overbeck & Tilak, 1998). Brain abnormalities reported in animal models of prenatal cocaine exposure include a reduction in number of cortical cells, inappropriate positioning of cortical neurons, altered glial morphology, reduction in length of neurites, and apoptotic neural cell loss (Lidow, 1995, 1998; Nassogne, Evrard, & Courtnoy, 1998). These changes are attributed, in part, to alternations in function of monoaminergic neurotransmitters that affect synaptogenesis, neural growth, and cell proliferation.

However, unlike early media reports of severe developmental consequences associated with cocaine use during pregnancy, research in humans has demonstrated that the sequelae of prenatal cocaine exposure are subtle but meaningful (Harvey & Kosofsky, 1998; Lester, LaGasse, & Seifer, 1998; Neuspiel, 1994; Vorhees, 1995). In terms of pregnancy outcome, a few consistent findings have emerged in studies with nondrug using control groups: higher risk for spontaneous abortion, shorter gestational age, smaller head circumference, shorter birth length and lower birth weight (Lester, Freier & LaGasse, 1995; Lutiger, Graham, Einarson, & Koren, 1991). In terms of neurobehavioral outcomes, no overall syndrome has been found in infants prenatally exposed to cocaine, in part due to methodological problems (Frank, Augustyn & Zuckerman, 1998; Lester, LaGasse & Bigsby, 1998). A review of ten studies using the BNBAS, one of the most consistent measures used, suggests that problems with state regulation occurs most

frequently (Frank, Augustyn & Zuckerman, 1998). State regulation, according to the theory underlying the development of the BNBAS, is the third developmental task of the first two months of life, which must be successfully negotiated before attention can be directed to stimuli in the external environment (Brazelton, 1984, 1994; Brazelton, Nugent & Lester, 1987; Nugent & Brazelton, 2000).

In terms of prenatal cocaine exposure's specific effect on attention, a number of animal models are suggestive. In a mouse model using Pavlovian conditioning and a blocking paradigm in which redundant information must be ignored, learning deficits and behavioral alterations suggestive of problems in selective attention were found (Kosofsky & Wilkins, 1998). Similarly, a primate model using rhesus monkeys also demonstrated problems in the acquisition of operant behaviors in cocaine-exposed offspring (Morris, Gillam, Allen & Paule, 1996). Impairments in attention and discriminative learning have been demonstrated in rabbits using a foot shock paradigm (Gabriel & Taylor, 1998).

In humans, a handful of studies have begun to emerge indicating that children prenatally exposed to cocaine begin to show problems with attention and that these problems become more evident after age 4 (Beckwith, Crawford, Moore & Howard, 1995; Chasnoff, Anson, Hatcher, Stenson, Iaukea & Randolph, 1998; Leech, Richardson, Goldschmidt & Day, 1999; Mayes, Grillon, Granger & Schottenfeld, 1998). A model for understanding the effects of prenatal cocaine exposure on child behavior, including attention has been presented by Lester, Freier and LaGasse (1995). As shown in Figure 1, cocaine is thought to affect neuroregulatory mechanisms, which in turn result in

disorders of behavioral regulation that manifest as the "Four A's of Infancy": attention, arousal, affect and action.

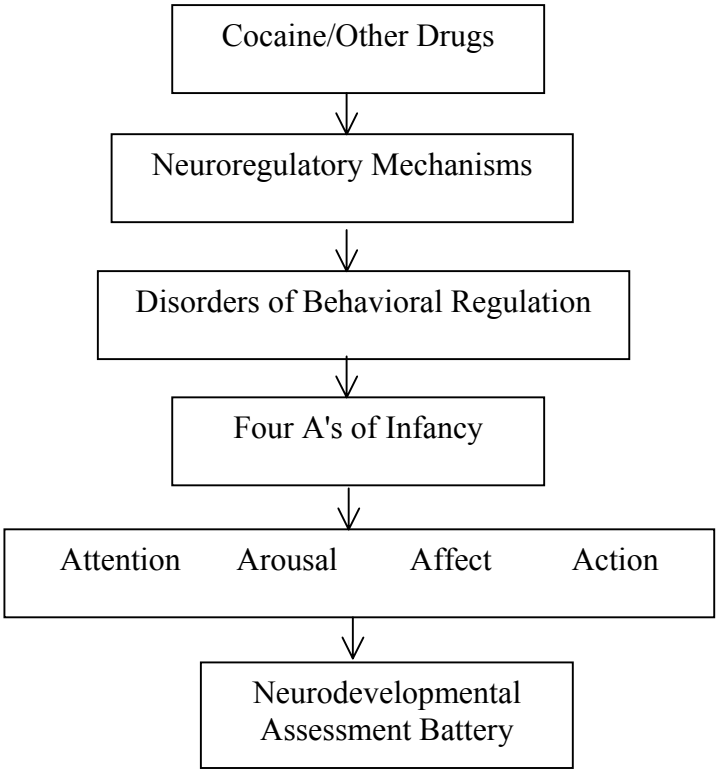

Figure 1-1. Theoretical model of the effects of prenatal cocaine exposure on child behavior taken from Lester, Freier and LaGasse (1995).

Relationship between Attention and Reading

Few theoretical models explicitly link the development of attentional abilities and the development of reading skills in children. Models of reading development generally focus on the processing of component skills in three areas: phonology, orthography, and semantics (Adams, 1994). A variety of investigations, including genetic studies, have examined the association between reading disability and Attention Deficit/Hyperactivity Disorder (ADHD); (Brock & Knapp, 1996; Felton & Wood, 1989; Fergusson & Horwood, 1992; Gilger, Pennington & DeFries, 1992; Javorsky, 1996; Light, Pennington,

Gilger & DeFries, 1995; Nahri & Ahonen, 1995; Robins, 1992; Velting & Whitehurst, 1997; Willcutt & Pennington, 2000). The overwhelming majority of these studies, however, have failed to distinguish subtypes with inattentive symptoms and hyperactivity. As Hinshaw (1992) pointed out in his review, while the link has been established between inattention and hyperactivity, on the one hand, and reading underachievement, on the other, causal models have rarely been tested using sufficient methodological controls. Only a small number of investigations have examined the relationship between attention and reading in children without diagnosed ADHD or reading disability (e.g., Velting and Whitehurst, 1997; Wood and Felton, 1994). Fortunately, two longitudinal investigations using large samples of normal children have begun to elucidate the relationship between attention and reading (Rabiner, Coie, & the Conduct Problems Prevention Research Group, 2000; Rowe & Rowe, 1992). Both of these longitudinal studies merit detailed review.

A longitudinal investigation by Rabiner and colleagues (2000) found that early attention problems predicted reading achievement even after controlling for prior reading achievement, IQ, and other behavioral problems. A heterogeneous group of children (N = 211) from four sites was followed from kindergarten through fifth grade. Attentional measures were collected from the children's teachers using the inattentive items from the Child Attention Problems Scale (Edelbrock, 1990) in kindergarten and the inattention scale of the ADHD Rating Scale (DuPaul, 1991) in grades 1 and 2. Reading achievement was measured in kindergarten and grade 1 using the Letter-Word Identification subtest from the Woodcock-Johnson Psychoeducational Battery-Revised (WJ-R, Woodcock & Johnson, 1991); reading achievement in grade 5 was measured using both the Letter-

Word Identification and Passage Comprehension subtests of the WJ-R. It was found that kindergarten reading was significantly correlated (r = -.29) with kindergarten inattention after controlling for IQ and parental involvement. First grade reading was also significantly correlated with first grade inattention (r = -.29) after controlling for IQ, parental involvement, and kindergarten reading and inattention scores. Inattention accounted for 6% of the total variance in kindergarten and first grade reading scores, comparable to the amount of variance explained by IQ. Fifth-grade reading was significantly correlated (r = -.10) with second grade inattention after controlling for all the previous variables—IQ, parental involvement, kindergarten reading and inattention and first grade reading and inattention. A path analysis using multiple regression procedures found that the model with all of the variables explained 66% of the variance in the children's fifth-grade reading achievement.

More importantly, the researchers found that children who were highly inattentive first graders (standardardized scores >1.0) were at greater risk for reading difficulties. Between kindergarten and first grade, the mean standardized reading achievement scores of the highly inattentive children declined significantly (-.52 to -.86), making them three times more likely than their peers to show a one standard deviation discrepancy criteria between IQ and reading ability. By fifth grade, the mean standardized reading score for the highly inattentive first graders remained substantially below the mean at .71.

Another longitudinal study by Rowe and Rowe (1992) used structural equation modeling in a sample of 5,092 normal students ages 5 to 14 years to investigate the relationship between inattentiveness in the classroom and reading achievement as mediated by family socioeconomic background factors, reading activity at home and

attitudes towards reading. A stratified sample of students was drawn from 256 classes in 64 public and 28 private elementary and secondary schools from four regions (two metropolitan and two rural) in Victoria, Australia, reflecting 91% of the target sample. Study measures were collected at five time points: year levels 1, 3, 5, 7, and 9. The family socioeconomic indicators used were number of years of mother's education and father's education and mothers' and father's occupational classification as measured on an 8-point scale. Students' reading activity at home was obtained from self-report responses to four questions measured on a four-point Likert-type scale while students' attitude toward reading was determined using three question measured on a 5-point Likert-type scale. For students ages 5 to 6 years, interviews were conducted with classroom teachers to assess reading activity and attitudes. Classroom inattentiveness at all ages was obtained from teacher responses to four items measured on a 5-point Likert-type scale. Assessment of reading achievement consisted of two measures: an age-appropriate reading comprehension test and teacher ratings on a criterion-referenced profile of student reading behaviors (Rowe & Rowe, 1992). Data were analyzed using four age categories: 5 to 6 years, 7 to 8 years, 9 to 11 years and 12 to 14 years.

Results indicated that across all age groups the measure of inattentiveness accounted for the largest proportion of variance, ranging from 13.4% to 22.9%. Attitudes towards reading and reading activity at home each explained between approximately 5% and 15%. The proportion of variance in reading achievement accounted by socioeconomic variables was very small, ranging from 0.3 to 3.2%. Analyses using a recursive structural equation model, in which all effects are unidirectional, indicated that inattentiveness has strong negative influences on students' reading achievement as well as

on the mediating variables of attitude towards reading and reading at home. Reading activity at home was found to have a significant influence on students' attitudes towards reading and acted as a strong mediator between inattentiveness and reading achievement that increased as students progressed through school. Socioeconomic status was found to have little influence on any of the other four factors in the model (Rowe & Rowe, 1992).

A second set of analyses was conducted using a non-recursive structural equation model to examine interdependent effects between inattentiveness and reading achievement. Goodness-of-fit indices were greater than .97 for all age groups, indicating that the model fit the data well. Reciprocal effects between inattentiveness and reading achievement were found to be significant and negative, and this relationship grew stronger over time. In sum, the two principal findings were that: 1) inattentive behaviors in the classroom have a significant negative influence on students' reading achievement and 2) reading achievement, mediated by the direct influence of attitudes toward reading and reading activity at home, has a stronger effect on reducing inattentive behaviors. Related to the second finding, the authors argue that low reading achievement leads to high inattentiveness (Rowe & Rowe, 1992).

The results of these two longitudinal studies converge on the notion that significant relationships exist between children's attentional abilities and their reading ability. Both studies also suggest that early intervention for inattentive children may help to reduce the chances of later reading problems. For children prenatally exposed to cocaine who may be at greater risk for attentional problems, early detection and intervention could have a significant impact on their academic and overall developmental

outcomes and highlights the need for more research on this potentially vulnerable population.

Study Purpose and Hypotheses

The purpose of the current study is to investigate the developmental trajectory of attention in a sample of children prenatally exposed to cocaine to determine: 1) whether: an indicator of attentional problems in infancy predicts poor attention skill in early childhood and 2) whether attentional measures at birth and early childhood are related to reading ability after controlling for the influence of general verbal ability and the caregiving environment.

It is hypothesized that after controlling for prenatal obstetric risk and exposure to alcohol, tobacco, and marijuana, the significant differences between children prenatally exposed to cocaine and matched controls on an early indicator of attention problems will persist at ages 5 and 7. More specifically, children prenatally exposed to cocaine will show worse performance on measures of attention than their matched controls. In addition, the poor performance of the exposed children will have direct and indirect negative effects on reading achievement at age 7 after controlling for verbal ability and the caregiving environment.

CHAPTER 2
METHODS

Participants

Participants in the current study were children enrolled in a prospective, longitudinal National Institute of Drug Abuse-funded study (DA 05854) to examine the effects of prenatal cocaine exposure on developmental outcomes. The original study, entitled Project C.A.R.E. (Cocaine Abuse in the Rural Environment), is housed at the University of Florida's Shands Teaching Hospital, and the study's principal investigators are Marylou Behnke, M.D. and Fonda Davis Eyler, Ph.D. In the original study, 154 cocaine-using pregnant women and 154 non-using matched controls were enrolled prospectively soon after they first contacted the health care system, either at a prenatal obstetric clinic or at the hospital. Detailed information regarding recruitment and enrollment of participants is provided in the Procedures section. Since enrollment in the longitudinal study, there has been a relatively low attrition rate (approximately 10%). All the children who participated in follow-up assessments at ages 5 and 7 and who have complete data for all the study measures were included in the present study.

A variety of data is available on the original study sample based on previous studies (Behnke, Eyler, Conlon, Wobie, Woods, & Cumming, 1998; Behnke, Eyler, Woods, Wobie, & Conlon, 1997; Eyler, Behnke, Conlon, Woods, & Wobie, 1998a, 1998b; Eyler, Behnke, Garvan, Woods, Wobie, & Conlon, 2001; Woods, Behnke, Eyler, Conlon & Wobie, 1995). Of the 154 cocaine users, 70% admitted to using crack, 16% used powder cocaine and 14% denied any cocaine use but had a positive urine screen.

Only 6% of the cocaine-using group of women received some form of drug treatment during pregnancy. The entire study sample was predominantly African American (*n* = 125), lowest Hollingshead socioeconomic status (SES) category (Hollingshead, 1995, *n* = 118) and had more than one child. As shown in Tables 2-1, 2-2, and 2-3, significant differences on a number of variables were found between the cocaine-using mothers and their babies when compared to their matched controls. First, the cocaine-using mothers were significantly older than the comparison group (27.4 years vs. 22.8 years, $p = .0001$). However, there were no differences between the groups based on the number of women in the over 40 years age range, which has been associated with increased perinatal risk (Eyler et al., 1998a). Second, the cocaine-using mothers entered prenatal care significantly later than the non-using mothers. However, multiple regression analyses controlling for alcohol, tobacco, and marijuana use showed that only tobacco use significantly predicted when the mothers entered prenatal care (Eyler et al., 1998a). Third, the Hobel Total and Perinatal Risk Scores were significantly higher for the cocaine-using mothers, and the difference in the Hobel Total Risk Score was due to higher Prenatal Risk Scores. There were no significant differences between groups on the Labor and Delivery and Neonatal Risk Scales (Eyler et al., 1998a). The fourth difference between the groups was in the proportion of mothers who used other substances during their pregnancies. Significantly more cocaine-using mothers also used tobacco, alcohol, and marijuana compared to their matched controls. Lastly, the number of infants born before 37 weeks gestation was significantly higher among the cocaine-using mothers, but there was no significant difference in mean gestational age between the two groups of infants as calculated using the method of Dubowitz, Dubowitz, and Goldberg (1970) (*M*

= 38.3 weeks, *SD* = 2.7 for cocaine-exposed, *M* = 38.7 weeks, *SD* = 2.9 for non-exposed; *p* = .24) (Eyler et al., 1998a).

For the neonates, significant differences on all four growth measures—birth weight, length, head circumference, and chest circumference—were found between those with prenatal cocaine exposure (PCE) and those without PCE. However, the Ponderal Index (Kliegman & King, 1983), calculated using the standard formula birth weight (grams) divided by length $(cm)^3$, did not differ between groups although the infants with PCE had significantly lower birth weights and significantly shorter birth lengths as compared to the infants without PCE (Eyler et al., 1998a). In multiple regression analyses using cocaine, marijuana, alcohol, and tobacco, no single drug or combination of drugs was a significant predictor of the Ponderal Index. In contrast, with head and chest circumference, there was an interaction between cocaine and tobacco such that the infants of mothers who used both were significantly smaller than the infants of mothers who did not use tobacco, who only used tobacco, or who used cocaine but did not use tobacco (Eyler et al., 1998a).

Measures

Four sets of variables were used in the current study: demographic variables, a birth outcome measure, measures of cognitive development at age 5 and 7, and caregiving environment measures. The demographic variables, also called exogenous variables, were of interest for the current study because of their potential relationship with child cognitive development. The six demographic variables were: amount of prenatal drug exposure (cocaine, alcohol, tobacco, and marijuana), Hobel prenatal obstetrical risk score, and gender. Child ethnicity was excluded as a variable since the overwhelming majority of the sample (more than 75%) is African American, the two

study groups were matched for socioeconomic status, and it is necessary to limit the number of variables for the analyses planned. In terms of birth outcome measures, head circumference at birth has been shown to be predictive of later outcomes in several studies (Chasnoff, Griffith, Freier, & Murray, 1992; Eyler, Behnke, Garvan, Wobie, & Hou, 2002). Data from 21 child cognitive measures collected at birth, age 5, and age 7 were also used in the current study: 12 attention measures, 8 verbal ability measures, and 2 reading ability measures. Finally, 7 measures of the caregiving environment gathered at age 5 and age 7 were included to examine the relative contribution of the home environment to child cognitive development. Table 2-4 provides a summary of the all of the variables used in the study, the construct they were designed to assess, and the ages at which they were assessed.

Demographic Variables

Prenatal drug exposure. Maternal use of cocaine, alcohol, tobacco, and marijuana was obtained using a drug history interview procedure adapted from that of Day, Wagener, and Taylor (1985). Detailed information about the drug history interview procedure is provided in the Procedures section. Prenatal cocaine exposure was operationalized as a ratio of the number of weeks of reported cocaine use divided by the total number of weeks of each gestation plus 3 months prior to gestation (the period covered by the substance use interview). Prenatal alcohol exposure was quantified using the average number of ounces of absolute alcohol consumed per day throughout pregnancy. Similarly, the average number of cigarettes smoked per day and the average number of marijuana joints smoked per day throughout the pregnancy were used to measure prenatal tobacco and prenatal marijuana exposure, respectively.

Head circumference. Orbitofrontal head circumference for each child measured in centimeters using a plastic coated tape.

Hobel Obstetric Risk Scale (Hobel, Hyvarinen, Okada, & Oh, 1973). The Hobel provides a quantitative assessment of 125 prenatal, intrapartum and neonatal factors that are associated with perinatal morbidity and death. For the current study only the Hobel Prenatal Risk Score was used as it was found to differ between the cocaine-using mothers and the comparison mothers in the original sample from which the participants were drawn (Eyler et al., 1998a). Scores are assigned clinically to 50 historical and developing prenatal items; 40 early, interim, and late intrapartum factors; and 35 neonatal factors. Weights of 1, 5, or 10 are assigned to each of the factors based on their assumed relationship to perinatal morbidity and death. The initial validity of the Hobel Obstetrical Risk scale was demonstrated in a sample of 738 mixed high- and low-risk pregnancies using theoretically assigned weights to each of the variables (Hobel, Hyvarinen, Okada, & Oh, 1973). Validity was further established in a larger sample of 1,417 mixed high- and low-risk pregnancies (that included the 738 cases from the previous sample) by comparing the clinically assigned weights to those derived from a logistic regression model (Hobel, Youkeles, & Forsythe, 1979). In this latter study, the clinically assigned scores had a true positive classification rate of 82.5% and a true negative classification rate of 49.5%, which compared favorably with the logistic model's predictions. In a review of obstetric risk-scoring systems, Wall (1988) reported that the Hobel system has a sensitivity of .504 and .669, specificity of .685 and .701, and positive predictive validity of .228 and .293 for the antepartum period and the intrapartum periods, respectively.

Measures of Cognitive Development

Attention Measures

Brazelton Neonatal Behavioral Assessment Scale (BNBAS; Brazelton, 1984). Three BNBAS cluster scores, Habituation, Orientation, and Regulation of State, were used as measures of infant attention after birth. The BNBAS is a widely used instrument for assessing the neurobehavioral responses of the newborn to his or her new extrauterine environment. It is designed as an interactive assessment for use with newborns from 36 to 44 weeks gestational age. The BNBAS consists of 28 behavioral items scored on a nine-point scale and 21 reflex items scored on a four-point scale. The behavioral items examine behaviors such as response to visual, auditory and tactile stimulation, orientation, alertness, activity, and irritability. Central to the behavioral assessment is the newborn's state of consciousness—deep sleep, light sleep, drowsy quiet alert, active alert or crying—which serves as the foundation for evaluating his or her sensory and motor responses. The scoring summary divides the items into four general domains of functioning; however, a seven-cluster scoring method has been developed based on conceptual and empirical methods. The seven BNBAS clusters are: Habituation, Orientation, Motor, Range of State, Regulation of State, Autonomic Stability, and Reflexes. Psychometrically, test-rest reliability is difficult to establish for the BNBAS due to rapid changes in the organization of the neonate's behavior during the first few days and weeks. The BNBAS requires extensive training to obtain interrater reliability of .92 as recommended by the manual. The validity of the BNBAS has been established by more than 25 years of clinical and research use (Brazelton, 1984).

Integrated Visual and Auditory Continuous Performance Test (IVA CPT; Sandford & Turner, 1994; Sandford, 1995). The two IVA CPT composite scores for the visual modality, the Visual Attention Quotient (VAQ) and Visual Response Control Quotient (VRCQ), were used as measures of attention at ages 5 and 7. The visual attention composite scores were chosen over the auditory attention composite scores since the other attention measures in the study—Letter Cancellation, Trail Making Test, and the WISC-III Coding subtest—all rely primarily on the visual modality. Test protocols were reviewed to determine valid profiles based on the IVA CPT manual criteria. The VAQ is a composite score comprised of three raw scores: Focus (response variability), Vigilance (omission errors) and Speed (mean reaction time for all correct trials). The VRCQ is a composite score also derived from three raw scores: Prudence (impulsivity), Consistency (response variability), and Stamina (mean reaction time for correct responses to the first 200 and last 200 trials).

The IVA CPT is a 13-minute test of attention for children and adults designed to provide data for differentiating between the subtypes of Attention Deficit/Hyperactivity Disorder specified in the Diagnostic and Statistical Manual-4th Edition (DSM-IV; American Psychiatric Association, 1994). The IVA CPT measures responses to 500 intermixed visual and auditory stimuli spaced 1.5 seconds apart. The task involves responding by clicking a computer mouse when the stimulus is a visual or auditory 1 and inhibiting responses when the stimulus is a visual or auditory 2. The stimuli are presented in pseudo-random order in five sets of 100 trials with each set consisting of two 50-trial blocks. The blocks are counterbalanced between visual and auditory stimuli and between frequent presentation of target stimuli (designed to elicit impulsivity) and infrequent

presentation of target stimuli (designed to elicit inattentiveness). Overall, the IVA CPT yields six composite quotient scores on two factors (Response Control and Attention) and 22 raw scores which comprise a Fine Motor Regulation (Hyperactivity) scale, three Attribute scales, and six Validity scales (Sandford, 1995).

Limited demographic information about the normative sample for the IVA CPT is available from the manual. The sample consisted of volunteers (*N* = 487, males = 210, females = 277) ranging in age from five to 90 years. Individuals in the normative sample were not known to have past neurological disorders or current psychological, learning, attentional problems or to demonstrate hyperactivity. In addition, the normative sample was screened for medications other than birth control and nasal sprays and was not currently active in psychotherapy or counseling. Significant gender differences were found on two scales: males had faster reaction times but females made fewer commission (impulsive) errors. In addition, significant age effects for mean reaction time for correct responses followed a U-shaped curve. The test appears to be more demanding for younger children, as a rapid improvement (reduction in reaction time) was seen for children between the ages of 5 and 7. Reaction time continues to improve between 8 and 12 years of age then plateaus between the mid-teen to young adult years. Reaction time was fairly stable through middle age and then slowed down slightly after age 45. Normative information in the computerized database that accompanies the test is reportedly divided into "appropriate" age and sex groups (Sanford, 1995).

The limited information available about the psychometric properties of the IVA CPT suggests that it has adequate reliability and validity. The IVA CPT's test-retest reliability was studied using 70 normal volunteers (43 females, 27 males) between 5 and

70 years of age (mean age = 21.8 years). Correlation for a one- to four-week interval between test administrations for the Visual Attention Quotients was very strong at .75. For the visual attention Validity and Attribute scores, the correlations ranged from .34 to .80. Validity studies on the IVA CPT were conducted in a small sample of 26 children, ages 7 to 12, diagnosed by a physician or psychologist as having ADHD and a comparison group of 31 children with no known neurological, learning, emotional or ADHD related problems. Results indicated that IVA CPT shows excellent sensitivity, specificity, positive predictive power, and negative predictive power: 92%, 90%, 89% and 93%, respectively. Concurrent validity was established by comparing the IVA CPT to two other continuous performance tests and two rating scales. The IVA CPT showed 90% to 100% agreement with these other measures and had the lowest false positive rate at 7.7% (Sandford, 1995).

Letter Cancellation (Diller, Ben-Yishay, Gerstman, Goodin, Gordon, & Weinberg, 1974). The Letter Cancellation task time to completion is used as a measure of attention at ages 5 and 7. Mirsky et al. (1991) found, in both adults and children, that the Letter Cancellation test loaded on the "focus-execute" factor of attention in their three-factor model of attention. In addition to attention, the Letter Cancellation test is thought to assess visual scanning, motor speed, and activation and inhibition of repetitive motor responses (Lezak, 1995). The task consists of crossing out a target character that is randomly interspersed approximately in an array of at least five different characters. Three scores can be derived based on speed (time to completion), number of omission errors, and number of commission errors. The Letter Cancellation test has been found to be sensitive to a variety of problems in brain-damaged subjects, including spatial neglect

in right hemisphere stroke patients and temporal processing difficulties of left hemisphere stroke patients (Lezak, 1995).

Trail Making Test (TMT; Reitan & Wolfson, 1985). The TMT Trails A time to completion is used as measure of attention at age 7. The TMT is one subtest in the Halstead-Reitan Neuropsychological Test Battery and consists of two parts labeled Part A and Part B. The TMT is thought to measure a variety of functions including attention, visual scanning, sequencing, mental flexibility, and motor speed and agility (Lezak, 1995; Spreen & Strauss, 1999).

In Part A, the subject is instructed to draw lines to connect circles containing numbers scattered randomly on a page in numerical order. In Part B, the participant must draw lines alternately between circles containing numbers and circles containing letters in numerical and alphabetical order. Only Part A will be used since a meta-analysis of four studies of children ages 9 to 14 found that Part B may be less reliable in younger children (Leckliter, Forster, & Klonoff, 1992). Scoring for the test is based on time to completion.

In adult studies using a variety of patient populations (except those with schizophrenia), the reliability coefficients generally range from .64 to .94 (Spreen & Strauss, 1998). Mirsky et al. (1991) found using principal component analysis on test scores from a mixed sample of adults that both Parts A and B of the TMT loaded most highly on a “perceptual-motor speed” factor (.70 and .63, respectively), corresponding to their Focus-Execute component of attention; however, there were also significantly secondary loadings on a “vigilance” factor (.43 and .45 for Parts A and B, respectively), corresponding to their Sustain component of attention.

Wechsler Intelligence Scale for Children-Third Edition (WISC-III, Wechsler, 1991). The WISC-III Coding and Digit Span subtests were used as a measure of attention at age 7. The WISC-III is a well-validated test of general cognitive functioning for children ages 6 years to 16 years, 11 months. The test was standardized on a national sample of 2,220 children stratified by age, sex, race/ethnicity, geographic region and parent education according to the 1988 U.S. Census. The WISC-III has demonstrated good psychometric properties. The validity of the WISC-III is based, in part, on the numerous criterion-related studies conducted on its predecessor, the WISC-R. Factor analytic studies as well as correlational studies with three other Wechsler Scales (the WISC-R, WPPSI-R and WAIS-R), other ability tests, neuropsychological tests, and school grades support the validity of the WISC-III. In addition, the data on the WISC-III has been collected using samples of exceptional children (gifted, mentally retarded, learning disabled, and speech/language delays) and clinical groups (Attention Deficit/ Hyperactivity Disorder, severe conduct disorder, and epilepsy) (Wechsler, 1991).

The reliability coefficient for the Coding subtest at age 7 is .70 with an average reliability of .79 for the range of age 6 to 15 years. Validity for the Coding subtest is based on its factor analytic studies showing that correlates with a Processing Speed factor rather than Verbal or Performance factors. Additionally, in a factor analytic study of child attention measures, Mirsky et al. (1991) found that the number correct on the Coding subtest loaded on their "focus-execute" factor of attention along with number of omissions and time to completion on a Digit Cancellation task.

Verbal Ability

Wechsler Intelligence Scale for Children-Third Edition (WISC-III; Wechsler, 1991). The WISC-III Comprehension, Information, Similarities, and Vocabulary subtests

were used as measures of verbal ability at age 7. Reliability coefficients for the four subtests ranged from .72 to .79 for the 7-year-olds in the normative sample, and .67 for the composite Verbal Comprehension factor (*N* = 200). The validity of the Information, Comprehension, Vocabulary, and Similarities subtests as measures of verbal ability is based on the moderate intercorrelations between the subtests (ranging from .46 to .64 for 7-year-olds in the normative sample), as well as factor analytic studies showing that the four subtests load together on the same factor (Verbal Comprehension). Again, the overall reliability and validity of the WISC-III is based on extensive research on its predecessor, the WISC-R, correlational studies with other tests of ability and neuropsychological tests, and studies using various special populations.

Wechsler Preschool and Primary Scale of Intelligence—Revised (WPPSI-R; Wechsler, 1989). The WPPSI-R Comprehension, Information, Similarities, and Vocabulary subtests were used as measures of verbal ability at age 5. The WPPSI-R is a well-validated test of general cognitive functioning designed for children ages 3 years to 7 years, 3 months. The test was standardized on a national sample of 1,700 children stratified by age, sex, race/ethnicity, geographic region and parent education and occupation based on survey data gathered by U.S. Census Bureau in 1986. The WPPSI-R has demonstrated good psychometric properties. For the age group of interest (5 years), split-half reliability coefficients range from .59 to .86 for the individual subtests. Stability coefficients during a test-rest interval of 3 to 7 weeks (*N* = 175) for the individual subtests ranged from .53 to .81. The overall validity of the WPPSI-R is based, in part, on studies of its predecessor, the WPPSI. In addition, the WPPSI-R has been evaluated using factor analytic studies and correlational studies with the WISC-R, Stanford-Binet

Intelligence Scale-Fourth Edition (Thorndike, Hagen, & Sattler, 1986), the McCarthy Scales of Children's Abilities (McCarthy, 1972) and the Kaufman Assessment Battery for Children (Kaufman & Kaufman, 1983). Validity studies of the WPPSI-R have also been conducted using samples of gifted, mentally deficient, learning disabled and speech/language impaired children (Wechsler, 1989).

Reading Ability

Wechsler Individual Achievement Test (WIAT; Wechsler, 1992). The WIAT Basic Reading and Reading Comprehension subtests were used as measures of reading ability at age 7. The Basic Reading subtest has 55 items covering picture naming, vocabulary, and single word reading. The Reading Comprehension subtest consists of 38 items that require the examinee to read a short passage and answer questions presented orally by the examiner. The WIAT is a well-validated test of academic achievement for children ages 5 years to 19 years, 11 months. The test was standardized on a national sample of 4,252 children stratified by age, sex, race/ethnicity, geographic region and parent education according to the 1988 U.S. Census (N = 331 for the age group of interest, 7 years). A subgroup of 1,284 children from the WIAT standardization sample was also administered one of the Wechsler intelligence scales. For the age group of interest (7 years), 100 children were administered both the WIAT and the WISC-III. A weighting procedure was used to assure that the scores for the subgroup were comparable to those of the WISC-III standardization sample.

The WIAT consists of eight subtests; however, only the psychometric properties of the Basic Reading and Reading Comprehension subtests will be reviewed here. Overall, both subtests have demonstrated good psychometric properties. For 7-year-olds, the split-half reliability coefficients for the Basic Reading and Reading Comprehension

subtests are .95 and .93, respectively. Stability coefficients for the Basic Reading and Reading Comprehension subtests are .91 and .89 for grade 1 ($N = 76$) and .94 and .90 for grade 2 ($N = 74$), respectively. Reliability and stability coefficients are even higher for the overall Reading Composite, which is comprised of the two subtests. The age 7 reliability coefficient for the Reading Composite is .97, and grade 1 and grade 2 stability coefficients are .95 and .96.

The content validity of the WIAT is based on reviews by curriculum experts and empirical item analysis studies. The WIAT's construct and criterion-related validity was determined by correlational studies using the WIAT subtests and other individually-administered achievement tests. Across a variety of ages, the Basic Reading and Reading Comprehension subtests were found to correlate from .79 to .87 (median = .82) with the analogous subtests in five other achievement test batteries including the Wide Range Achievement Test-Revised (Jastak & Wilkinson, 1984) and the Woodcock-Johnson Psycho-Educational Battery-Revised Tests of Achievement (Woodcock & Johnson, 1991). Both subtests also have significant correlations (>.40) with school grades in a sample of children ages 6 to 19 years ($N = 867$). In addition, studies of special groups of children (including those identified as gifted, or having mental retardation, emotional disturbance, learning disabilities, Attention Deficit Hyperactivity Disorder, and hearing impairment) support the validity of the WIAT (Wechsler, 1992).

Caregiving Environment Measures

Home Observation for Measurement of the Environment (HOME; Caldwell & Bradley, 1984). Seven subscales of the HOME were used as measures of the child's caregiving environment at ages 5 and 7. HOME scores were determined by observation by trained interviewers during interviews with the child caregivers in their homes. The

four subscales of the Early Childhood version of the HOME (EC HOME) most closely related to literacy development—Learning Stimulation, Language Stimulation, Learning Stimulation, and Variety in Experience—were used to assess the caregiving environment at age 5. The three subscales of the Middle Childhood version of the HOME (MC HOME) most related to literacy development—Growth Fostering Materials and Experiences, Provision for Active Stimulation, and Family Participation—were used to assess the caregiving environment at age 7. The HOME is a screening measure that assesses factors related to the nurturance and stimulation in a child's home environment that are believed to be important for cognitive development. The HOME was designed as an alternative to sociodemographic factors for identifying children at "high risk" for intellectual/academic problems. Scores are based on both the observer's visual inspection of the home and self-report of the child's primary caregiver obtained through a semi-structured interview during a 45- to 90-minute home visit. The HOME has been found to be significantly correlated with longitudinal cognitive test performance and academic achievement in children ages 3 to 10 years (Bradley, Caldwell, & Rock, 1988; Bradley, 1994; Bradley & Whiteside-Mansell, 1998).

Four forms of the HOME are available: an Infant-Toddler version (ages birth to 3 years), an Early Childhood version (ages 3 to 6 years), a Middle Childhood version (ages 6 to 10 years), and an Early Adolescent version (ages 10 to 14 years). Since the Early Childhood (EC) and Middle Childhood (MC) versions were used in the present study, only they are reviewed here. The EC HOME contains 55 items clustered in eight subscales: 1) Learning Materials, 2) Language Stimulation, 3) Physical Environment, 4) Parental Responsivity, 5) Learning Stimulation, 6) Modeling of Social Maturity, 7)

Variety in Experience, and 8) Acceptance of Child. The MC HOME contains 59 items clustered into eight subscales: 1) Parental Responsivity, 2) Physical Environment, 3) Learning Materials, 4) Active Stimulation, 5) Encouraging Maturity, 6) Emotional Climate, 7) Parental Involvement, and 8) Family Participation.

The various versions of the HOME and their subscales have undergone name changes, reorganization, or both and over time. However, no significant changes in the number of items or item content have been made for the EC HOME and MC HOME. When the data from the EC HOME were collected in the current study, it was called the "Preschool" version. Since the structure of the items has not changed since the scale was renamed, the current names for the EC HOME subscales will be used throughout this study. Of the four EC HOME subscales used in the current study, only two were relabeled when the parent scale was renamed. The Language Stimulation and Variety in Experience subscales remained the same while the Learning Materials subscale was previously labeled "Learning Stimulation" and the current Learning Stimulation subscale was called "Academic Stimulation."

The MC HOME, called the "Elementary" version when the data for this study were collected, underwent reorganization of its items into eight subscales rather than seven subscales. The three subscales used in the current study were not affected by this structural change. Thus, the current names for the MC HOME subscales will be used throughout the study. Of the three MC HOME subscales used in the current study, one was relabeled when the parent scale was renamed. The Learning Materials subscale was previously called "Growth Fostering Materials and Experiences."

All four versions of the HOME have been found to have good psychometric properties. Test-retest reliability, as measured by coefficient alpha, is above .90 for the total scores and is generally higher for the longer than the shorter subscales. Interobserver agreement is reported as 90% or higher for all versions. Concurrent and predictive validity studies have shown that the HOME is significantly correlated with IQ, as high as $r = .58$. Low to moderate correlations (.30 to .60) between EC HOME scores and children's contemporaneous and later intellectual and academic performance have generally been found (Bradley, 1994). Similar relationships have been reported for MC HOME scores and children's school performance and classroom behavior (Bradley, Caldwell, Rock, Hamrick, & Harris, 1988). These relationships have been found in African American as well as European American samples (Bradley & Caldwell, 1981; Bradley, Rock, Caldwell, Harris & Hamrick, 1987). While HOME scores have low to modest correlations with a wide variety of demographic variables including race, family structure, neighborhood, and maternal age, two studies have shown that no single demographic factor accounts for much of the variance in HOME scores and that all the demographic factors together only account for about 50% of the variance (Bradley & Caldwell, 1981; Bradley, Mundfrom et al., 1994).

Procedure

Detailed information regarding participant recruitment and assessment of birth outcome measures is provided in Eyler et al. (1998a, 1998b) and is summarized here. Recruitment of participants took place between July 1991 and July 1993 with the last child born in February, 1994. Institutional Review Board approval was obtained for study procedures and incentives. Informed consent was carefully obtained for all participants, including those who were illiterate. The consent process included an explanation of child,

maternal, and family measures, drugs tests and interviews, the Federal Certificate of Confidentiality, and the distinction between the researchers and clinical providers in assurance of confidentiality. All participants were recruited from women designated to deliver at Shands Teaching Hospital, a tertiary care center.

Exclusion criteria included rare but major maternal illnesses diagnosed before pregnancy that are known to affect pregnancy or developmental outcome, such as diabetes, sickle cell disease, and mental retardation, as well as women who abused legal drugs or used any illicit drugs other than cocaine and marijuana. In addition, only mothers who spoke English and were equal to or greater than 18 years of age were consented for enrollment in the study.

A priori participant matching criteria were developed during the original longitudinal study to minimize the effect of possible confounding variables on pregnancy or child outcomes. Four matching criteria for the control group were chosen, three of which were based on characteristics that significantly differed between prenatal cocaine users and the general obstetric population and which have been shown to relate to pregnancy or developmental outcome. These three matching criteria were: 1) the level of Hollingshead Index of SES, 2) racial/ethnic group membership (African American versus other racial/ethnic categories), and 3) number of previous births (multiparous or primiparous). The fourth matching criteria, location of prenatal care, was chosen to equate groups on risk factors or complications that developed during, but not before, pregnancy. This variable included the local public health unit, outlying clinics (which sent only high-risk women to deliver at Shands) or no prenatal care.

The researchers approached 2,526 potential participants of whom 85% gave informed consent to participate in the study. Most cocaine-using participants were enrolled prenatally (75%) from the two closest county public health prenatal clinics or from the hospital's high-risk referral prenatal clinic by approaching all non-excluded potential participants. The additional participants were recruited when they arrived to deliver at the hospital. This latter group consisted of women who had received no prenatal care or those whom the researchers had been unable to interview in the prenatal clinic. Of the 2,526 potential participants, 179 were approached for consent at delivery and 89% gave informed consent. The 372 refusals included 13 women who were willing to give consent for the study but were unable or unwilling to provide a urine specimen at enrollment required for continued participation. After the first interview, 22 of the women who consented (11 cocaine users and 11 nonusers who would have been potential matches) were eliminated from study. Most (n = 16) were found to have used excluded illicit drugs, while three reported using confounding prescription medications and another three were no longer able to deliver at Shands Teaching Hospital.

As each cocaine-using woman who consented and met exclusion criteria was identified, one or two participants from the pool who consented, who denied prenatal cocaine use, and whose urine specimens showed no evidence of cocaine use were selected for each match category. The oldest matched control from the appropriate category was then used as the final match. The two final groups of participants consisted of 154 cocaine-using women and 154 non-users.

The drug use interview, adapted from that of Day, Wagener, and Taylor (1985), was administered by a one of a number of well-trained, non-judgmental interviewers who

attempted to establish rapport after informed consent was given by the maternal participant. Interviewers carefully read and explained all portions of a detailed drug history due to the low literacy level of the mothers enrolled in the study. Interviews were conducted at the end of each trimester, whenever possible, and details about drug use during the previous three months was probed in order to induce less guilt for the participants. Women with very late or no prenatal care were interviewed after birth about drug use throughout their pregnancy. Enrollment rates at the end of the first trimester, the end of the second trimester, and at delivery were: 41% (41 cocaine; 84 control), 34% (61 cocaine, 44 control) and 25% (69 cocaine, 9 control), respectively. To trigger memory around real-time events, calendars were used to help women recall their drug use history within the context of her pregnancy. In addition to cocaine, participants were queried about their use of drugs from several categories, including marijuana, alcohol, tobacco, and other illicit drugs (the latter for exclusion purposes) using street or slang drug names. The amount (or cost) and timing of each woman's usual use of each drug were recorded. Increases and decreases in usage patterns were also noted in order to calculate a more accurate average use per trimester.

Urine specimens were obtained for drug screening on two occasions that could not be anticipated by the participants. The first specimen was collected on the day of enrollment in the study. Women who consented but refused to provide a urine specimen on the same day were dropped from the study. The second specimen was obtained from the mother on the day of the baby's birth if an infant specimen was unavailable. A full toxicology screen of the urine was conducted using fluorescence polarization

immunoassay. Positive drug screens were then confirmed with gas chromatography/mass spectroscopy.

Study measures were administered to the children and their mothers or another primary caregivers at several different assessments. Throughout the course of the longitudinal study, all of the measures have been administered by trained, certified, or licensed professionals blinded to the study group membership of the mother and child. In the rare cases when a tester was unmasked, other backup testers were used for the assessments.

The first set of child assessments occurred shortly after birth. Infants were evaluated within the first day or as soon as they were well in the Shands Hospital Clinical Research Center, which provided controlled conditions of light, sound, and temperature. In a few cases in which the infants were unstable, they were evaluated in the nursery. Orbitofrontal head circumference measurements were obtained by one of a team of neonatal nurse practitioners blinded to the drug history of the mother. The Hobel Obstetric Risk Scores were determined postdelivery by medical personnel trained by one of the larger study's principal investigators, Marylou Behnke, M.D. The BNBAS was administered midway between feedings as close to 40 weeks postconceptual age as possible. In the current sample the majority of infants (69%) were evaluated within 24 hours after birth. Another 20% were administered the BNBAS within 48 hours after birth. The BNBAS was administered by certified, reliable evaluators blinded to the drug history of the mothers.

The second set of assessments took place when the children were approximately 5 years old. The Early Childhood Home Observation for Measurement of the Environment

(EC HOME) was completed by one of two trained female interviewers during interviews conducted with the primary caregivers in the family's home. The age 5 cognitive test battery, including the IVA, Letter Cancellation, and WPPSI-R verbal subtests, was administered by one of two licensed school psychologists in private practice who were blinded to the child's group membership. Administration of the cognitive battery took place on the Project Care bus while it was parked either on the grounds of the child's school or outside the child's home. There was no significant difference in the mean age at which the two study groups were administered the age 5 test battery [$t(240) = .08$, $p = .93$] The combined average of the groups' ages were 5.34 years at the time of the first cognitive test battery.

The third sets of assessments occurred when the children were approximately 7 years old. The Middle Childhood Home Observation for Measurement of the Environment (MC HOME) was completed during interviews conducted with the primary caregivers in the family's home by the same interviewers who conducted the age 5 interviews. The age 7 speech and language assessment, which included the Wechsler Individual Achievement Test (WIAT) reading subtests, was administered following a physical examination by one of two licensed nurse practitioners blinded to the child's group membership. The age 7 speech and language assessment was completed by on the Project Care bus while it was parked on the grounds of the child's school or outside the child's home. The age 7 cognitive test battery also took place on the Project Care bus and was typically done within a day or two of the physical exam and speech and language assessment. The same two blinded, licensed school psychologists who administered the age 5 cognitive test battery also gave the age 7 cognitive test battery. The children were

provided breaks, including snacks, routinely and as needed during administration of the test batteries. There were no significant differences in the mean age at which the two study groups were administered the age 7 speech and language or cognitive test batteries [*t*s(240) = 1.04, .40, *p*s = .30, .69, respectively]. The combined averages of the groups' ages were 7.31 and 7.29 years during the speech and language and cognitive batteries, respectively.

After assessment protocols were reviewed for scoring accuracy, the scores for each participant were hand-entered into a Microsoft Access database. To minimize input errors, the data were entered a second time and checked against the original input. Discrepancies between the two sets of entries were reconciled by checking the protocols.

Age-corrected scaled scores for the WPPSI-R and WISC-III verbal ability subtests and age-corrected standard scores for the WIAT reading subtests were used. For age 5 Letter Cancellation, age 7 Letter Cancellation and TMT Trail A, time in seconds to complete the task was used. Raw scores were used for the EC and MC Home subscales. For structural equation modeling (SEM), it is not necessary for all of the variables to be in the same metric as the solution can be standardized by setting factor variances to one.

Hypotheses

Based on a review of the relevant literature, three a priori hypotheses were developed to examine the relationship between prenatal cocaine exposure and the development of attention and reading skills in children:

1. Performance on the BNBAS Habituation, Orientation, and State Regulation Supplementary Scales will be significantly correlated with performance on age 5 and 7 attention measures for both groups of children in the study.

2. Children with prenatal cocaine exposure (PCE) will perform significantly worse than matched controls on: a) attentional measures at age 5 (IVA CPT and Letter Cancellation), b) attentional measures at age 7 (IVA CPT, Letter Cancellation,

TMT Part A, WISC-III Coding, and WISC-III Digit Span), and c) reading measures at age 7 (WIAT Basic Reading and Reading Comprehension subtests).

3. It is hypothesized, regardless of significant group differences on measures of attention and reading, that performance on attentional measures at birth, age 5, and age 7 will be significant predictors of reading at age 7 after controlling for verbal ability and the caregiving environment. It is hypothesized that PCE will have both a direct effect on attention and an indirect effect on attention that is mediated by birth head circumference. It is also hypothesized that PCE will have an indirect effect on reading at age 7 that is mediated through attention.

Data Inspection and Analyses

Data Screening

The first step in the data analysis plan involved screening the data for violations of normality and for missing values. Data screening was conducted using SPSS and PRELIS 2.52 (Jöreskog & Sörbom, 2001b). With the exception of the four drug variables, data with significant skewness, kurtosis, or both were transformed into normal scores. The drug variables were not transformed as it was expected that these data would not have a normal distribution.

Missing Data

A large number of missing values were found for the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) Habituation, Orientation, and Regulation of State scores. Specifically 83 participants (n = 39 for PCE group, n = 44 for non-exposed group) were missing the Habituation score, 45 participants were missing the Orientation score (n = 30 for PCE group, n = 15 for non-exposed group), eight were missing both the Habituation and Orientation scores (n = 5 for the PCE group, n = 3 for the non-exposed group), and 20 participants were missing all three scores (n = 15 for PCE group, n = 5 for non-exposed group). As reported in Eyler et al. (1998b), a significantly larger proportion of infants with PCE than non-exposed infants failed to come to a quiet, alert state so that

the Orientation items could be administered (25% vs. 12%). Independent sample *t*-tests using Bonferroni correction for multiple comparisons were conducted between the groups of children with missing BNBAS scores and the rest of the sample. Results indicated no significant differences between the groups missing the Habituation score, Orientation score, or both scores and the rest of the sample on any of the demographic variables, head circumference, or gestational age. For the group missing all three BNBAS scores, one significant difference was found from the rest of the sample. There was a larger proportion of African Americans in the group missing all three BNBAS scores than in the rest of the sample [$t(26) = -2.41$, $p = .019$]. It was decided to use all available BNBAS data to evaluate the first hypothesis but to exclude the BNBAS from the path analysis needed to evaluate the third hypothesis.

A number of missing values were also found for the Intermediate Visual and Auditory Continuous Performance Test (IVA CPT) Visual Attention Quotient (VAQ) and Visual Response Control Quotient (VRCQ) scores at both ages 5 and 7. Specifically, 17 children were missing the IVA CPT at age 5 ($n = 12$ for PCE group, $n = 5$ for non-exposed group), 17 children were missing the IVA CPT at age 7 ($n = 8$ for PCE group, $n = 9$ for non-exposed group), and one child (non-exposed) was missing both sets of IVA CPT scores. Independent sample *t*-tests using Bonferroni correction for multiple comparisons were conducted between the groups of children with missing IVA CPT scores and the rest of the sample. Results indicated no significant differences between the groups at age 5 or at age 7 on any of the demographic variables, head circumference, or measures of attention, reading, verbal ability, or the caregiving environment. It was

decided to use all available IVA CPT data to evaluate the second hypothesis but to exclude these data from the path analysis needed to evaluate the third hypothesis.

Not including the BNBAS or IVA CPT scores, 29 participants were found to be missing only one of the remaining 30 data points. The distribution of missing scores was as follows: Hobel prenatal risk score (n = 6), age 5 Letter Cancellation (n = 11), age 5 HOME Academic Stimulation subscale (n = 1), and age 7 Trail Making Test (TMT) Part A (n = 11). With the exception of the TMT, the missing data points appeared to be random, so the mean score based on the child's group membership (PCE vs. non-exposed) was substituted for the missing data.

For the TMT, the missing scores were generally the result of the child not being able to count to 15 or not being able to complete the practice item (n = 5 for PCE group, n = 6 for non-exposed group). Since it is somewhat unusual for a 7-year-old not to be able to count to 15, independent-samples t-tests between the group of children missing the TMT and the rest of the sample were conducted. Results revealed significant differences on 14 variables as shown in Table 2-4. A significant difference was found for ethnicity; all of the children who could not do the TMT Part A were African American. These children also scored significantly worse than the rest of the sample on the Hobel prenatal risk score; EC HOME Language Stimulation subscale; age 5 and age 7 Letter Cancellation; WPPSI-R Comprehension, Information, and Similarities; WISC-III Digit Span, Comprehension, Information, Similarities, and Vocabulary; and WIAT Basic Reading and Reading Comprehension. Since the differences between the group missing the TMT and the rest of the sample were significant, a decision was made to replace the

missing TMT Part A scores with a arbitrary score of 300 seconds, the time limit for discontinuance of the test.

Accounting for the Participants

After imputing values for participants who were missing only one data point, a total sample size of 240 participants (n = 120 for both groups) remained for further analyses. Thus, a total of 68 of the 308 participants originally enrolled in the prospective, longitudinal study were excluded from the current study. Of these 68 participants, 22 had more than one missing data point, 12 died prior to age 7, eight dropped out of the study, 10 were lost to follow up, six had moved out of the area, eight refused to participate in one or both of the age 5 and age 7 assessments, one child was deaf, and one child was profoundly retarded and could not complete the assessments.

To determine whether the differences found in the original study sample were also present in the smaller sample used in the current study, independent samples t-tests with Bonferroni correction for multiple comparisons were performed for the demographic variables and head circumference. Table 2-6 shows the results of the analyses, which revealed that the sample for the current study was very similar to the original sample. As in the original sample, the group with PCE had significant greater mean amounts of prenatal cocaine exposure [$t(238) = 17.43$, $p = .000$], prenatal alcohol exposure [$t(238) = 5.69$, $p = .000$], and prenatal tobacco exposure [$t(238) = 7.30$, $p = .000$] than the non-exposed group. In addition, the group with PCE had significantly higher mean Hobel prenatal risk score than the non-exposed group, as in the original sample [$t(238) = 5.11$, $p = .000$] and significantly smaller mean head circumference as compared to the non-exposed group [$t(238) = -3.26$, $p = .001$]. Finally, statistically similar proportions of

females and African Americans were found in both study groups [*t*s (238) = 1.42 and -1.20, *p*s = .156 and .232, respectively].

There were, however, two differences between the current sample and the original study sample. Unlike the original sample, there was no significant difference between the groups in mean amount of prenatal marijuana exposure [$t(238) = 2.06$, $p = .041$]. Another difference between the current sample and the original sample was the significantly shorter mean gestational age for the group with PCE compared to the non-exposed group [$t(238) = -3.27$, $p = .001$]. The average gestational age of the infants with PCE was 38.50 weeks compared to 39.29 weeks for the non-exposed infants. While statistically significant, the difference between the groups was less than one week.

Statistical Analyses

SPSS and LISREL 8.52 (Jöreskog & Sörbom, 2001a) were used to conduct all statistical analyses. The criterion for significance tests for all a priori hypotheses was set at $\alpha = .05$ with Bonferroni correction for multiple comparisons. To test the first hypothesis, a correlational analysis was conducted to determine whether the BNBAS is significantly related to measures of attention at age 5 and age 7. To test the second hypothesis of group differences on measures of attention and reading, a cross-sectional analysis using the independent samples *t*-test was conducted. Finally, to test for longitudinal associations between measures of attention administered at birth, age 5 and age 7 and reading ability at age 7 and the hypothesis that head circumference mediates the effect of PCE on attention and reading, structural equation modeling (SEM) was used in a combined sample of the children with PCE and without PCE.

SEM is a powerful statistical technique that involves multiple regression analyses of factors. Factors, called latent constructs, were derived from the reliable shared variance of one or more observed variables indicators and thus are free of measurement error. SEM allows for the examination of complex relationships between multiple continuous and discrete independent variables and multiple continuous and discrete dependent variables. After specification of a model, which is a type of confirmatory factor analysis, SEM can be used to test a model, test specific hypotheses about a model (including mediational hypotheses), modify an existing model, or test a set of related models (Ullman, 2001).

To ensure sufficient identification to conduct structural equation modeling (SEM), the number of unknown parameters must be less than or equal to the number of known pieces of information supplied to the program. In general, then, the number of indicator variables should be limited. In addition, to analyze longitudinal data, a stable number of participants are required across all time points. For the 18 participants who were randomly missing one of the variables in the study, the missing data was imputed using the mean score based on group membership (PCE vs. non-exposed). For the 11 participants who were missing the TMT, an arbitrary score of 300 seconds, the time limit for discontinuance of the test, was substituted for the missing value. Participants missing more than one data point were excluded from the analyses.

Figures 2-1 and 2-2 provide diagrams of the proposed structural model of the longitudinal relationship between PCE, attention, and reading. Eight of the factors in the model are indicated by a single variable: prenatal cocaine exposure (COCAINE), prenatal alcohol exposure (ALCOHOL), prenatal tobacco exposure (TOBACCO), prenatal

marijuana exposure (MARIJUA), Hobel prenatal risk (HOBEL), sex (SEX), head circumference at birth (HEADC), Letter Cancellation at age 5 (LCAN5), and Digit Span at age 7 (DSPAN7). Attention at age 5 is singly indicated by Letter Cancellation (LCAN5). Attention at age 7 was divided into two separate factors. Digit Span was allowed to be a singly indicated factor (DSPAN7) because it does not have a visuomotor component while the other three attentional measures—Letter Cancellation, TMT Part A, and WISC-III Coding subtest—which have a visuomotor component were combined into a Visual Attention factor (VATTN7). The age 5 caregiving environment factor (HOME5) was indicated by four subscales from the EC HOME while the age 7 caregiving environment factor (HOME7) was indicated by three subscales from the MC HOME. The age 5 and age 7 Verbal Ability factors (VERBAL5 and VERBAL7) were indicated by the four age-appropriate Wechsler subtests—Comprehension, Information, Similarities, and Vocabulary.

The structure of the model was based on the predictive relationships that are expected to exist between the various factors. The six endogenous variables were used to predict birth head circumference, which in turn is used to predict the three age 5 factors (LCAN5, VERBAL5, and HOME5). As expected with longitudinal data, each of the three age 5 factors (attention, verbal ability, and caregiving environment) was used to predict their respective age 7 factors. As the only measure of attention obtained at age 5, Letter Cancellation factor was used to predict the two age 7 attention factors, DSPAN7 and VATTN7. The other two age 5 factors, VERBAL5 and HOME5, are used to predict their respective age 7 factors, VERBAL7 and HOME7. Finally, the four age 7 factors

(DSPAN7, VATTN7, VERBAL7, and HOME7) were used to predict the final outcome, age 7 reading ability (READ7).

Table 2-1 Continuous Variables that Differed Significantly Between Mothers in the Two Original Study Groups

Variable	Group[a]				*p*-value
	Cocaine Users		Matched Controls		
	M	*SD*	*M*	*SD*	
Age	27.6	4.8	23.8	5.5	.0001***
Week entered prenatal care	14.8	7.6	12.1	7.2	.003**
Total Hobel score	94.2	72.1	78.5	48.2	.0276*
Prenatal Hobel score	54.5	20.1	43.0	19.3	.00001***

[a]n = 154 for both groups.
* $p < .05$, ** $p < .01$, *** $p < .001$, two-tailed using the independent samples *t*-test.

Table 2-2 Non-continuous Variables that Differed Significantly Between Mothers in the Two Original Study Groups

Variable	Group[a]		*p*-value
	Cocaine Users	Matched Controls	
Tobacco users	123	37	.0001***
Alcohol users	118	47	.0001***
Marijuana users	68	11	.0001***
Births < 37 weeks gestation	28	14	.03*

[a]n = 154 for both groups.
* $p < .05$, ** $p < .01$, *** $p < .001$, two-tailed using the independent samples *t*-test.

Table 2-3 Variables that Differed Significantly Between Neonates in the Two Original Study Groups

Variable	Group[a]				*p*-value
	Cocaine-Exposed		Matched Controls		
	M	*SD*	*M*	*SD*	
Birth weight (g)	2985	668	3179	700	.03*
Length (cm)	48.7	3.2	49.7	3.3	.007**
Chest circumference (cm)	31.6		33.6		.01*
Head circumference (cm)	33.6		34.8		.007**

[a]n = 154 in both groups.
* $p < .05$, ** $p < .01$, two-tailed using the independent samples t-test.

Table 2-4 Summary of Variables for Current Study

Variable Name	Variable Label	Construct Assessed	Age
	Demographic Variables		
WUCFULL	Average ratio of weeks of cocaine use	Cocaine exposure	prenatal + 3 months prior
POAALC	Average ounces of absolute alcohol consumed per day	Alcohol exposure	prenatal
POATOB	Average number of cigarettes smoked per day	Tobacco exposure	prenatal
POAMAR	Average number of marijuana joints smoked per day	Marijuana exposure	prenatal
HEADC	Head circumference	Head circumference	birth
HOBPRE	Hobel Prenatal Risk	Prenatal risk	birth
SEX	Sex	Sex	birth
	Child Cognitive Variables		
BRHABIT	BNBAS Habituation	Attention	<1 week
BRORIENT	BNBAS Orientation	Attention	<1 week
BRREGSTA	BNBAS Regulation of State	Attention	<1 week
IVAVAQ5	IVA CPT Visual Attention Quotient	Attention	5 years
IVAVRCQ5	IVA CPT Visual Response Control Quotient	Attention	5 years
LCANT5	Letter Cancellation time	Attention	5 years
IVAVAQ7	IVA CPT Visual Attention Quotient	Attention	7 years
IVAVRCQ7	IVA CPT Visual Response Control Quotient	Attention	7 years
LCANT7	Letter Cancellation time	Attention	7 years
TRAILA	TMT Trail A time	Attention	7 years
W3COD	WISC-III Coding	Attention	7 years

Table 2-4. Continued

Variable Name	Variable Label	Construct Assessed	Age
W3DSS	WISC-III Digit Span	Attention	7 years
WPCOM	WPPSI-R Comprehension	Verbal ability	5 years
WPINF	WPPSI-R Information	Verbal ability	5 years
WPSIM	WPPSI-R Similarities	Verbal ability	5 years
WPVOC	WPPSI-R Vocabulary	Verbal ability	5 years
W3COM	WISC-III Comprehension	Verbal ability	7 years
W3INF	WISC-III Information	Verbal ability	7 years
W3SIM	WISC-III Similarities	Verbal ability	7 years
W3VOC	WISC-III Vocabulary	Verbal ability	7 years
WIATBR	WIAT Broad Reading	Reading ability	7 years
WIATRC	WIAT Reading Comprehension	Reading ability	7 years
Caregiving Environment Variables			
H5LEAR	EC HOME Learning Materials	Home environment	5 years
H5LANG	EC HOME Language Stimulation	Home environment	5 years
H5ACAD	EC HOME Language Stimulation	Home environment	5 years
H5VARI	EC HOME Variety in Experience	Home environment	5 years
H7GROW	MC HOME Learning Materials	Home environment	7 years
H7ACTI	MC HOME Active Stimulation	Home environment	7 years
H7FAMI	MC HOME Family Participation	Home environment	7 years

Note. BNBAS = Brazelton Neonatal Behavior Assessment Scale, IVA CPT = Intermediate Visual and Auditory Continuous Performance Test, TMT = Trail Making Test, WISC-III = Wechsler Intelligence Scale for Children-Third Edition , WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence-Revised, WIAT = Wechsler Individual Achievement Test, EC HOME = Early Childhood Home Observation for Measurement of the Environment, MC HOME = Middle Childhood Home Observation for Measurement of the Environment.

Table 2-5 Significant Differences Between Participants With and Without TMT Part A Scores

Variable	Group[a]				*p*-value
	With TMT		Without TMT		
	M	*SD*	*M*	*SD*	
Ethnicity[b]	.82	.38	1.00	.00	.000***
Hobel prenatal risk score	49.83	20.50	41.36	11.64	.042*
EC HOME Language Stimulation	6.36	.96	5.73	1.49	.038*
Letter Cancellation - age 5 (secs.)	102.53	43.30	131.09	38.78	.033*
WPPSI-R Comprehension	7.92	2.48	5.27	1.19	.001**
WPPSI-R Information	7.22	2.48	4.18	1.25	.000**
WPPSI-R Similarities	7.85	2.24	5.91	1.97	.005**
Letter Cancellation - age 7 (secs.)	58.70	20.94	80.27	28.89	.001**
WISC-III Digit Span	8.94	2.59	4.18	1.47	.000*
WISC-III Comprehension	8.20	3.27	4.90	2.47	.001**
WISC-III Information	8.17	2.54	4.81	.98	.000***
WISC-III Similarities	8.27	4.49	3.00	2.45	.000***
WISC-III Vocabulary	8.44	2.62	5.00	2.41	.000***
WIAT Basic Reading	96.52	12.35	82.82	1.47	.000***
WIAT Reading Comprehension	92.24	11.67	0.64	2.91	.000***

Note. EC HOME = Early Childhood Home Observation for Measurement of the Environment, TMT = Trail Making Test, WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence-Revised, WISC-III = Wechsler Intelligence Scale for Children-Third Edition, WIAT = Wechsler Individual Achievement Test.
[a]n = 229 for group with TMT scores, n = 11 for group without TMT scores.
[b]Ethnicity was coded so that African American = 1 and others = 0. Thus, the number in the table represents the proportion of the group that was African American.
* $p < .05$, ** $p < .01$, *** $p < .001$, two-tailed using the independent samples *t*-test and Bonferroni correction for familywise error rate.

Table 2-6 Demographic Variables Comparing Groups in Current Study

Variable	Group[a]				*p*-value
	PCE		Non-exposed		
	M	*SD*	*M*	*SD*	
Prenatal cocaine exposure	.458	.288	.000	.000	.000***
Prenatal alcohol exposure	.232	.414	.002	.005	.000***
Prenatal tobacco exposure	8.96	9.23	1.86	5.33	.000***
Prenatal marijuana exposure	.009	.369	.002	.127	.041*
Hobel prenatal risk score	55.79	19.66	43.09	18.84	.000**
Gestational age (weeks)	38.50	2.10	39.29	1.61	.001*
Head circumference (cm)	33.49	1.93	34.24	1.66	.001**
Sex[b]	.52	.50	.43	.50	.156
Ethnicity[c]	.80	.40	.86	.35	.232

Note. PCE = prenatal cocaine exposure.
[a]*n* = 120 for both groups.
[b]Sex was coded so that female = 1, male = 0. Thus, the numbers in this row indicate the proportion of the group that was female.
[c]Ethnicity was coded so that African American = 1, others = 0. Thus, the numbers in this row indicate the proportion of the group that was African American.

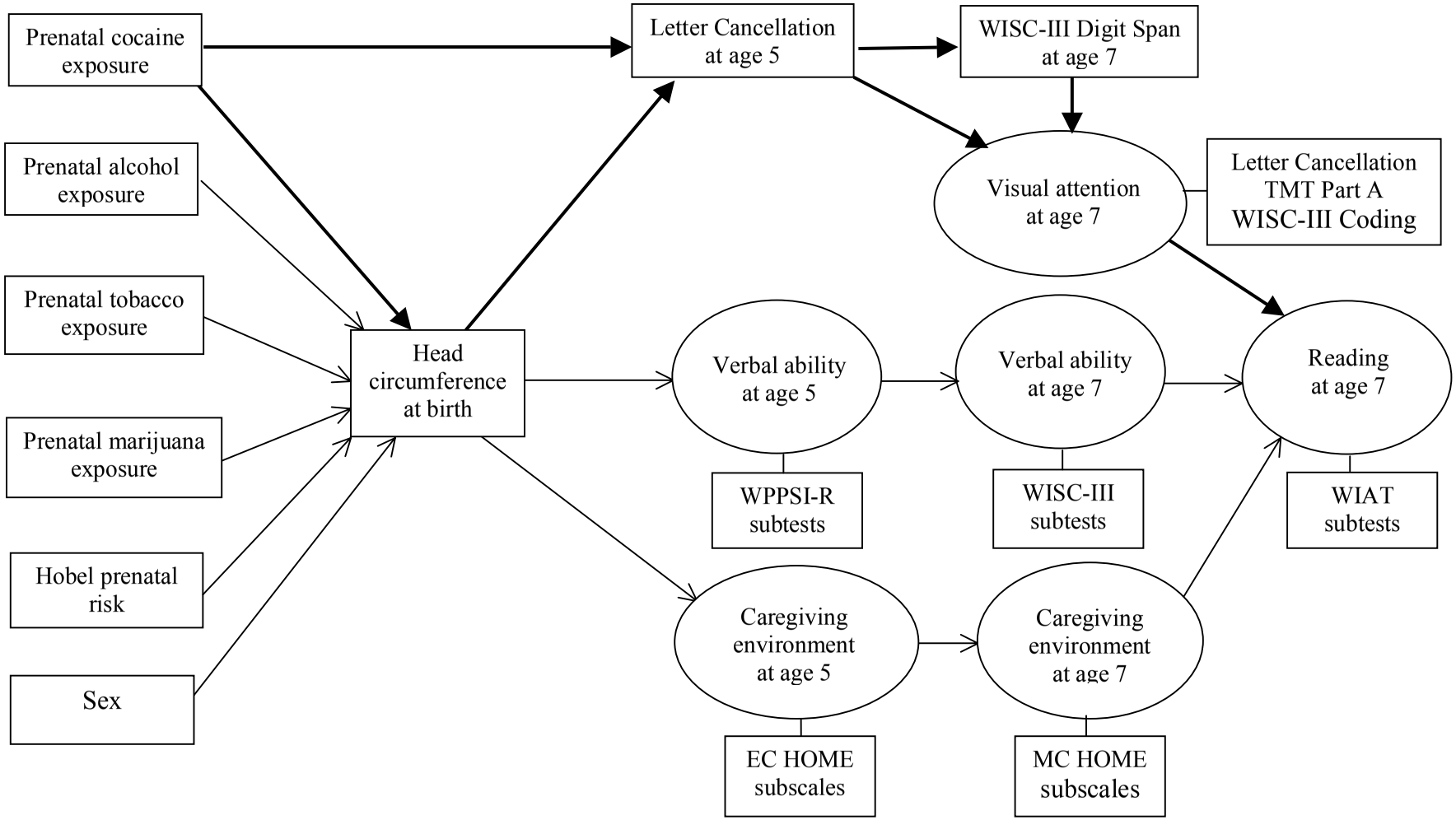

Figure 2-1. Proposed structural equation model with factors and indicators for relationships between prenatal cocaine exposure, birth head circumference, attention, and reading while controlling for other prenatal drug exposure, Hobel prenatal risk, sex, verbal ability, and caregiving environment. Primary relationships of interest are indicated by bold lines. Ellipses indicate latent variables (factors) while boxes indicate measured variables. BNBAS = Brazelton Neonatal Behavioral Assessment Scale. EC HOME = Early Childhood Home Observation Measurement of the Environment. MC HOME = Middle Childhood Home Observation Measurement of the Environment. IVA CPT = Intermediate Visual and Auditory Continuous Performance Test. TMT = Trail Making Test. WIAT = Wechsler Individual Achievement Test. WISC-III = Wechsler Intelligence Scale for Children-Third Edition. WPPSI-R = Wechsler Primary and Preschool Scale of Intelligence - Revised.

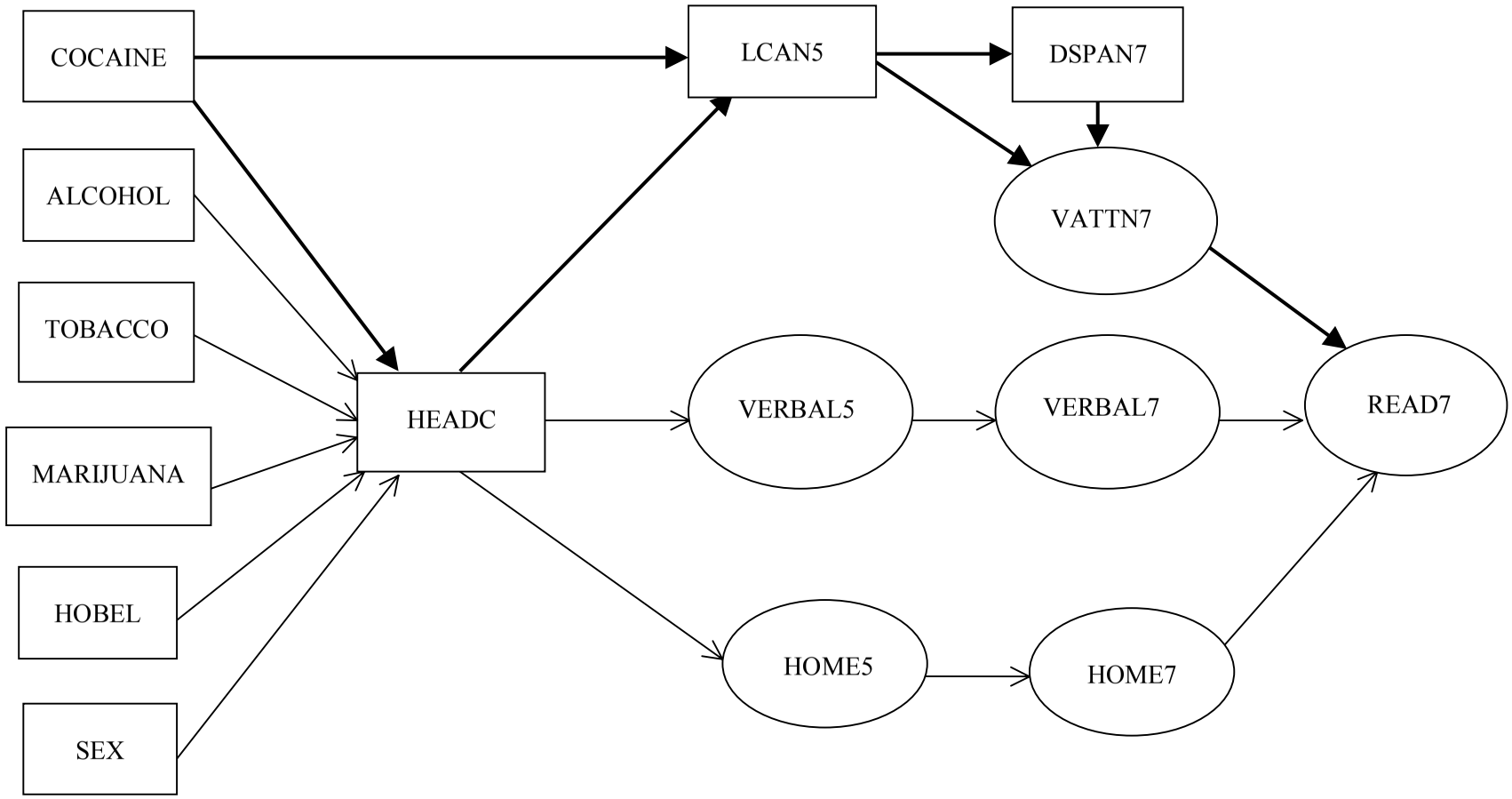

Figure 2-2. Proposed structural equation model with factor names for relationships between prenatal cocaine exposure, birth head circumference, attention, and reading while controlling for other prenatal drug exposure, Hobel prenatal risk, sex, verbal ability, and caregiving environment. Primary relationships of interest are indicated by bold lines. COCAINE = prenatal cocaine exposure, ALCOHOL = prenatal alcohol exposure, TOBACCO = prenatal tobacco exposure, MARIJUANA = prenatal marijuana exposure, HOBEL = Hobel prenatal risk score, SEX = child sex, HEADC = head circumference at birth, LCAN5 = Letter Cancellation at age 5, VERBAL5 = verbal ability at age 5, HOME5 = caregiving environment at age 5, DSPAN7 = Digit Span at age 7, VATTN7 = visual attention at age 7, VERBAL7 = verbal ability at age 7, HOME7 = caregiving environment at age 7, and READ7 = reading ability at age 7.

CHAPTER 3
RESULTS

Hypothesis #1. To test the first hypothesis—that the BNBAS Habituation, Orientation, and Regulation of State scores obtained during the first week of life would have significant relationships with measures of childhood attention at ages 5 and 7—a correlational analysis was performed using all available data for both groups. There was only one significant correlation between one of the BNBAS measures and one of the early childhood attention measures. The BNBAS Orientation score was significantly correlated with the age 5 IVA CPT visual attention quotient; while significant, this association was small ($r = .149$, $p < .05$, $N = 191$). No significant relationships were found between the three BNBAS scores and Letter Cancellation at age 5, or any of the age 7 attention measures (Letter Cancellation, IVA CPT scores, TMT Part A, WISC-III Coding, or WISC-III Digit Span). Intercorrelations between all of the proposed attention measures in the study for the combined sample of children with PCE and non-exposed children are shown in Table 3-1.

A post-hoc analysis was conducted to examine the relationship of the BNBAS Orientation score with the age 5 IVA CPT visual attention quotient separately by group (PCE vs. non-exposed). When analyzed separately by group, the relationship between the BNBAS Orientation score and the age 5 IVA CPT visual attention quotient became non-significant. However, it appears that the significant relationship found in the combined sample was driven largely by the PCE group ($n = 80$, $r = .217$, $p = .053$) rather than the non-exposed group ($n = 111$, $r = .095$, $p = .32$).

Hypothesis #2. To evaluate the second hypothesis that children with PCE would perform significantly worse than non-exposed children on measures of attention at ages 5 and 7 and on measures of reading at age 7, independent samples *t*-tests with Bonferroni correction for multiple comparisons were performed. As shown in Table 3-2, no significant differences were found between the groups on any of the attention or reading measures. For age 5 Letter Cancellation, the PCE group took an average of 108 seconds to complete the task, compared to 100 seconds for the non-exposed group [$t(238) = 1.44$, $p = .15$]. For each of the age 7 attention measures, the PCE and non-exposed groups obtained remarkably similar mean scores. For Digit Span and Coding, the scaled scores for the PCE group were 8.71 and 10.14, respectively, while the scores were 8.73 and 10.56 for the non-exposed group, respectively [*t*s(238) = -.06, and -.93, *p*s = .95 and .35, respectively]. For the other two time-based measures, Letter Cancellation and TMT Part A, the PCE group completed the tasks in 60 and 52 seconds on average while the non-exposed group required 59 and 54 seconds on average [*t*s(238) = -.36 and -.21, *p*s = .71 and .83, respectively]. Finally, on the two reading measures, both groups performed in the average range, with the PCE group having slightly higher means scores than the non-exposed group. Scaled scores were 96.20 and 95.59 for the Basic Reading subtest and 92.02 and 91.39 for the Reading Comprehension subtest for the PCE and non-exposed groups, respectively (*t*s(238) = .39 and .42, *p*s = .70 and .68).

Post hoc comparisons between the two groups were made for the remainder of the study variables using independent samples *t*-tests with Bonferroni corrections for multiple comparisons. As shown in Table 3-3, only two statistically significant group differences were found. One was for the EC HOME Learning Stimulation subscale [$t(238)$ 2.62, $p = .01$]; the other was for the MC HOME Growth Fostering Materials subscale [$t(238) = 3.12$, $p = .00$].

Ironically, the PCE group scored slightly higher than the non-exposed group on both measures. The PCE group obtained average scores of 7.41 for the EC HOME Learning Stimulation subscale and 5.11 for MC HOME Growth Fostering Materials subscale compared to respective means of 6.58 and 4.67 for the non-exposed group. This disparity is likely due to the fact that a significantly larger proportion of the children with PCE were living in placements away from their biological mothers at age 5 compared to non-exposed children (64% vs. 9%). Since there was only two significant between-groups differences, combining the PCE and non-exposed groups for all further analyses was deemed appropriate to maximize statistical power.

Hypothesis #3. To evaluate the third set of hypotheses that a) performance on measures of attention will be significant predictors of performance in reading, b) PCE will have a direct effect on attention and an indirect effect on attention mediated by head circumference, and c) PCE will have an indirect effect on reading mediated by attention, structural equation modeling (SEM) was performed on the combined sample of children with and without PCE. As noted earlier, the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) and Intermediate Visual and Auditory Continuous Performance Test (IVA CPT) were dropped from these analyses due to large numbers of missing data.

The first step in SEM is the development of the measurement model that, by definition, allows all the factors in the model to be correlated. Several indices were used to assess the goodness-of-fit of both the measurement and structural models. One index used was the ratio between the chi-square statistic and the degrees of freedom for the model. Generally, a model is considered to fit well if chi-square is less than twice the degrees of freedom ($\chi^2 < 2df$). Other indices used to assess fit in the current study are Jöreskog and Sörbom's (1989) goodness-of-fit (GFI), Bentler's (1990) normed comparative fit (CFI) and Bentler and Bonett's (1980)

nonnormed fit (NNFI) indices. For each of these indices, better fit is associated with higher values, and .90 is generally considered a minimum acceptable level (Bentler & Bonett, 1980). Finally, the root mean square error of approximation (RMSEA) takes into account the error of approximation in the population, while the root mean square residual (RMR) provides a measure of the average size of the residual difference between the actual covariances among the observed indicators and the covariances predicted by a particular model. For both the RMSEA and RMR, a value of ≤ 0.05 is considered an indicator of good fit (Browne and Cudeck, 1993; Bryant and Yarold, 1995).

The initial measurement model was checked for signs of underidentification including negative variances, correlations greater than 1.0, and factor loadings or correlations that seemed to have the wrong sign or were much smaller or much larger than expected. No signs of model underidentification were detected. Table 3-4 shows fit indices for the iterative process used to determine the final measurement model. The basic measurement model (M1), in which all variables were allowed to correlate, fit the data very well: χ^2 (281, N = 240) = 376.72, GFI = .90, CFI = .98, NNFI = .98, RMSEA = .04, and RMR = .05. No modifications of the measurement model were needed since all of the fit indices met their respective criteria for good fit.

The next step in SEM is construction of a structural model that fits the data as well as the final measurement model with fewer estimated parameters. The hypothesized structural model (S1) also fit the data moderately well [χ^2 (345, N = 240) = 536.37, GFI = .87, CFI = .97, NNFI = .96, RMSEA = .05, and RMR = .09] but significantly worse than the final measurement model. An iterative process was undertaken to improve the model's fit first by dropping insignificant paths one at a time, then inspecting the modification indices to determine additional parameters to freely estimate. Table 3-4 displays the fit indices of the intermediate models between the

initial hypothesized structural model and the final structural model. In the first four model steps, insignificant paths were dropped between the following factors: 1) Hobel and Head Circumference, 2) Head Circumference and age 5 Letter Cancellation, 3) Head Circumference and age 5 caregiving environment, and 4) age 7 Digit Span and Reading. As expected, these changes did not significantly improve the fit of the model but did increase the degrees of freedom for subsequent tests of model fit.

In the fifth model step (S6), a path was added between age 5 Verbal Ability and age 7 Digit Span, revealing a moderate relationship between the two factors ($\beta = .52$). Adding this path significantly improved the model fit as compared to the previous structural model: χ^2 difference (1, $N = 240$) = 41.53, $p = .00$. Further modifications were still needed, however, because the structural model was still significant different from the measurement model: χ^2 difference (67, $N = 240$) = 120.53, $p = .00$. In the sixth model step (S7), the insignificant path between age 5 Letter Cancellation and age 7 Digit Span was dropped with no significant change in the model's fit.

In the seventh model step (S8), estimating the path between age 5 Verbal Ability and age 7 Visual Attention revealed another moderately strong relationship ($\beta = .47$). Again, estimating this additional path significantly improved the model fit: χ^2 difference (1, $N = 240$) = 25.09, $p = .00$. However, this model was still significantly different from the measurement model: χ^2 difference (67, $N = 240$) = 96.55, $p < .05$. In the final model step, a path was added between Sex to age 7 Visual Attention. The magnitude of this relationship was small ($\beta = .29$), indicating that girls performed better than boys on the visual attention measures (females were coded as 1, males were coded as 0). Adding this final path also significantly improved the model fit over the previous structural model: χ^2 difference (1, $N = 240$) = 15.74, $p = .00$). No further attempts were

made to improve the fit of the structural model since it was no longer differed significantly from the measurement model: χ^2 difference (66, N = 240) = 80.81, p > .05).

The final structural model fit the data well [χ^2 (347, N = 240) = 457.53, GFI = .89, CFI = .98, NNFI = .98, RMSEA = .04, and RMR = .06] and was a significant improvement over the initial hypothesized structural model with improvements in all five fit indices. It should be noted, however, that two of the fit indices did not meet the criteria for good fit: GFI was < .90 and the RMR was > .05. Nevertheless, the final structural model was able to account for 44% of the variance in the age 7 Visual Attention factor and 68% of the variance in the age 7 Reading factor. As predicted, the Visual Attention factor was the strongest predictor of age 7 Reading even after controlling for verbal ability and the caregiving environment (βs = .44, .41, and .14).

In summary, the first hypothesis that the BNBAS scores collected during the first week would be significantly correlated with early childhood measures of attention and reading could not be evaluated due to a large amount of missing data. The second hypothesis, that children with PCE would perform significantly worse than non-exposed children on measures of attention at ages 5 and 7 and reading at age 7, was not supported. There was mixed support for the third set of hypotheses regarding relationships between attention and reading, PCE and attention, and PCE and reading. Visual attention at age 7 was found to be the strongest predictor of reading at age 7; however, PCE had no direct relationship with attention at age 5 or 7. PCE was found to have an indirect effect on reading at age 7 mediated by head circumference at birth, verbal ability and visual attention.

Table 3-1 Intercorrelations Between All Attention Measures for Combined Sample

	1	2	3	4	5	6	7	8	9	10	11	12
1. BNBAS Habituation	--	.076	.090	.051	.051	.090	-.028	-.021	.070	-.023	.010	.058
2. BNBAS Orientation		--	.273**	.149*	.081	-.051	.033	-.019	-.014	-.069	.008	-.095
3. BNBAS State Regulation			--	.070	.018	-.087	.040	-.028	.003	-.118	.086	-.014
4. IVA CPT VAQ - age 5				--	.630**	-.122	.129	.071	.024	-.215**	.089	.216**
5. IVA CPT VRCQ - age 5					--	-.158*	.075	.000	-.056	-.178**	.020	.219**
6. Letter Cancel - age 5						--	-.127	-.152*	.204**	.298**	-.277**	.211**
7. IVA CPT VAQ - age 7							--	.374**	-.031	-.161*	.131*	.247**
8. IVA CPT VRCQ - age 7								--	-.009	-.100	.150*	.138*
9. Letter Cancel - age 7									--	.148*	-.284**	-.105
10. TMT Part A										--	-.205**	-.303**
11. WISC-III Coding											--	.185**
12. WISC-III Digit Span												--

Note. *n*s vary by cell due to missing data. BNBAS = Brazelton Neonatal Behavioral assessment Scale, IVA CPT = Intermediate Visual and Auditory Continuous Performance Test, VAQ = Visual Attention Quotient, VRCQ = Visual Response Control Quotient, TMT= Trail Making Test, and WISC-III = Wechsler Intelligence Scale for Children-Third Edition.
* $p < .05$, ** $p < .01$, two-tailed.

Table 3-2 Group Means and Standard Deviations for Early Childhood Attention and Reading Variables

Variable	Group[a]				*p*-value
	PCE		Non-exposed		
	M	*SD*	*M*	*SD*	
IVA CPT VAQ - age 5 [b]	44.96	30.31	49.12	27.01	.261
IVA CPT VRCQ - age 5 [b]	62.15	37.46	66.72	34.29	.323
Letter Cancellation – age 5 (secs.)	108.31	43.28	99.41	43.15	.112
IVA CPT VAQ - age 7[c]	56.31	18.32	58.04	20.87	.488
IVA CPT VRCQ - age 7 [c]	73.80	25.69	77.97	23.17	.183
Letter Cancellation – age 7 (secs.)	60.22	21.75	59.15	21.86	.705
TMT Part A (secs.)	54.92	51.16	57.2	63.08	.629
WISC-III Coding	10.14	3.62	10.56	3.32	.347
WISC-III Digit Span	8.71	2.79	8.72	2.68	.978
WIAT Broad Reading	96.34	12.04	95.43	12.79	.569
WIAT Reading Comprehension	92.22	11.48	91.20	11.87	.499

Note. PCE = prenatal cocaine exposure, IVA CPT = Intermediate Visual and Auditory Continuous Performance Test, VAQ = Visual Attention Quotient, VRCQ = Visual Response Control Quotient, TMT = Trail Making Test, WISC-III = Wechsler Intelligence Scale for Children-Third Edition, WIAT = Wechsler Individual Achievement Test.
[a]*n* = 120 for both groups for all measures except IVA CPT scores. [b]*n* = 116 for PCE group, *n* = 126 for nonexposed group, [c]*n* = 123 for both groups.

Table 3-3 Group Means and Standard Deviations for All Other Study Variables

Variable	Group[a]				*p*-value
	PCE		Non-exposed		
	M	*SD*	*M*	*SD*	
Caregiving Environment– age 5					
EC HOME Academic Stimulation	4.49	.81	4.41	.93	.456
EC HOME Language Stimulation	6.48	.89	6.19	1.07	.022
EC HOME Learning Stimulation	7.40	2.36	6.59	2.51	.010*
EC HOME Variety in Experience	6.39	1.54	6.17	1.31	.237
Caregiving Environment– age 7					
MC HOME Active Stimulation	3.80	1.89	3.67	1.77	.581
MC HOME Family Participation	6.38	2.08	6.48	2.10	.719
MC HOME Growth Fostering Materials and Experiences	5.12	1.65	4.45	1.53	.001**
Verbal Ability – age 5					
WPPSI-R Comprehension	7.87	2.43	7.71	2.57	.574
WPPSI-R Information	7.27	2.45	6.90	2.59	.259
WPPSI-R Similarities	8.92	2.52	8.46	2.42	.155
WPPSI-R Vocabulary	7.82	2.31	7.71	2.23	.698
Verbal Ability – age 7					
WISC-III Comprehension	7.86	3.36	8.24	3.25	.383
WISC-III Information	8.08	2.63	7.96	2.55	.723
WISC-III Similarities	8.05	4.32	8.00	4.80	.944
WISC-III Vocabulary	8.15	2.80	8.41	2.61	.462

Note. PCE = prenatal cocaine exposure, TMT = Trail Making Test, WIAT = Wechsler Individual Achievement Test, EC HOME = Early Childhood Home Observation for Measurement of the Environment, WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence-Revised, MC HOME = Middle Childhood Home Observation for Measurement of the Environment, WISC-III = Wechsler Intelligence Scale for Children-Third Edition.

[a]n = 120 for both groups.

* $p < .05$, ** $p < .01$, *** $p < .001$, one-tailed using the independent samples *t*-test and Bonferroni correction for familywise error rate.

Table 3-4 Fit Indices for Nested Sequence of Measurement and Structural Models

Model Step	χ^2	*df*	*p*	GFI	CFI	NNFI	RMSEA	RMR	COMPARISON TO M1 measurement model χ^2	*df*	*p*	Comparison to previous model χ^2	*df*	*p*
MEASUREMENT MODEL														
M1. Basic measurement model	376.72	281	.00	.90	.98	.98	.04	.05						
Structural Models														
S1. Hypothesized structural model	536.37	345	.00	.87	.97	.96	.05	.09	159.65	64	.00			
S2. Drop path from HOBEL to HEADC	538.30	346	.00	.87	.97	.96	.05	.09	161.58	65	.00	1.93	1	NS
S3. Drop path from HEADC to LCAN5	538.32	347	.00	.87	.97	.96	.05	.09	161.60	66	.00	.02	1	NS
S4. Drop path from HEADC to HOME5	538.77	348	.00	.87	.97	.96	.05	.09	162.05	67	.00	.45	1	NS
S5. Drop path from DSPAN7 to READ7	538.78	349	.00	.87	.97	.96	.05	.09	162.06	68	.00	.01	1	NS
S6. Add path from VERBAL5 to DSPAN7	497.25	348	.00	.88	.98	.97	.04	.07	120.53	67	.00	41.53	1	.00
S7. Drop path from LCAN5 to DSPAN7	498.36	349	.00	.88	.98	.97	.04	.08	121.64	68	.00	1.11	1	NS
S8. Add path from VERBAL5 to VATTN7	473.27	348	.00	.88	.98	.98	.04	.06	96.55	67	NS	25.09	1	.00
S9. Add path from SEX to VATTN7	457.53	347	.00	.89	.98	.98	.04	.06	80.81	66	NS	15.74	1	.00

Note. $N = 240$. GFI = goodness of fit index, CFI = comparative fit index, NNFI = non-normed fit index, RMSEA = root mean square error of approximation, RMR = root mean square residual, M = measurement model, S = structural model, VATTN7 = age 7 visual attention, HOME5 = age 5 caregiving environment, HOBEL = Hobel prenatal risk, HOME7 = age 7 caregiving environment, LCan5 = age 5 Letter Cancellation, DSPAN7 = age 7 Digit Span, READ7 = age 7 reading, VERBAL5 = age 5 verbal ability, VERBAL7 = age 7 verbal ability.

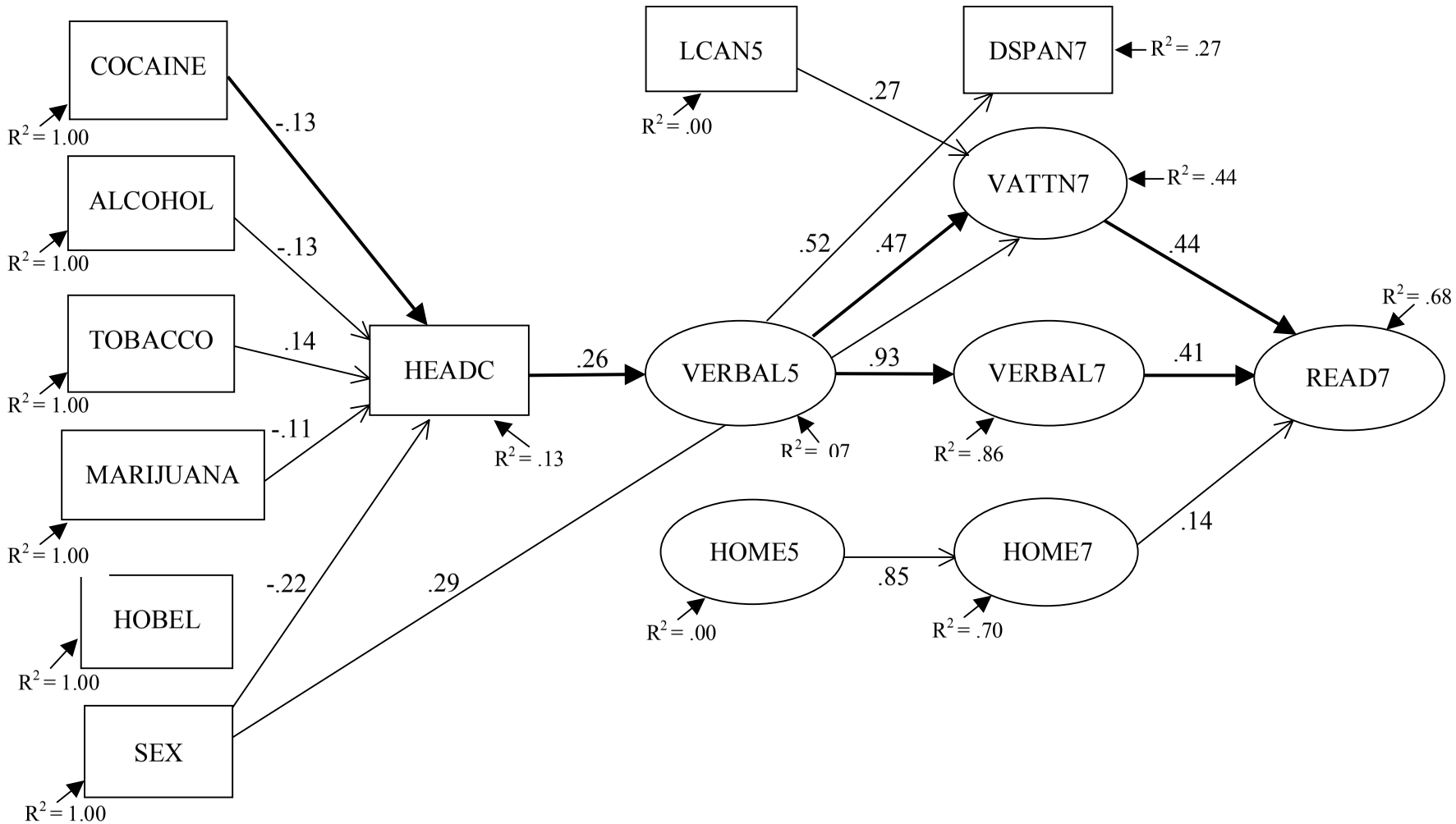

Figure 3-1. Final structural model of the relationship between prenatal cocaine exposure (COCAINE), other prenatal drug exposure (ALCOHOL, TOBACCO, and MARIJUANA), Hobel prenatal risk score (HOBEL), sex (SEX), birth head circumference (HEADC), age 5 Letter Cancellation (LCAN5), age 5 verbal ability (VERBAL5), age 5 caregiving environment (HOME5), age 7 Digit Span (DSPAN7), age 7 visual attention (VATTN7), age 7 verbal ability (VERBAL7), age 7 caregiving environment (HOME7), and age 7 reading ability (READ7). The bold lines highlight the effect of prenatal cocaine exposure (PCE) on age 7 reading, which is mediated through birth head circumference and verbal ability. Age 7 visual attention was the largest predictor of age 7 reading followed closely by age 7 verbal ability. Interestingly, sex was also a significant predictor of visual attention at age 7, with girls outperforming boys.

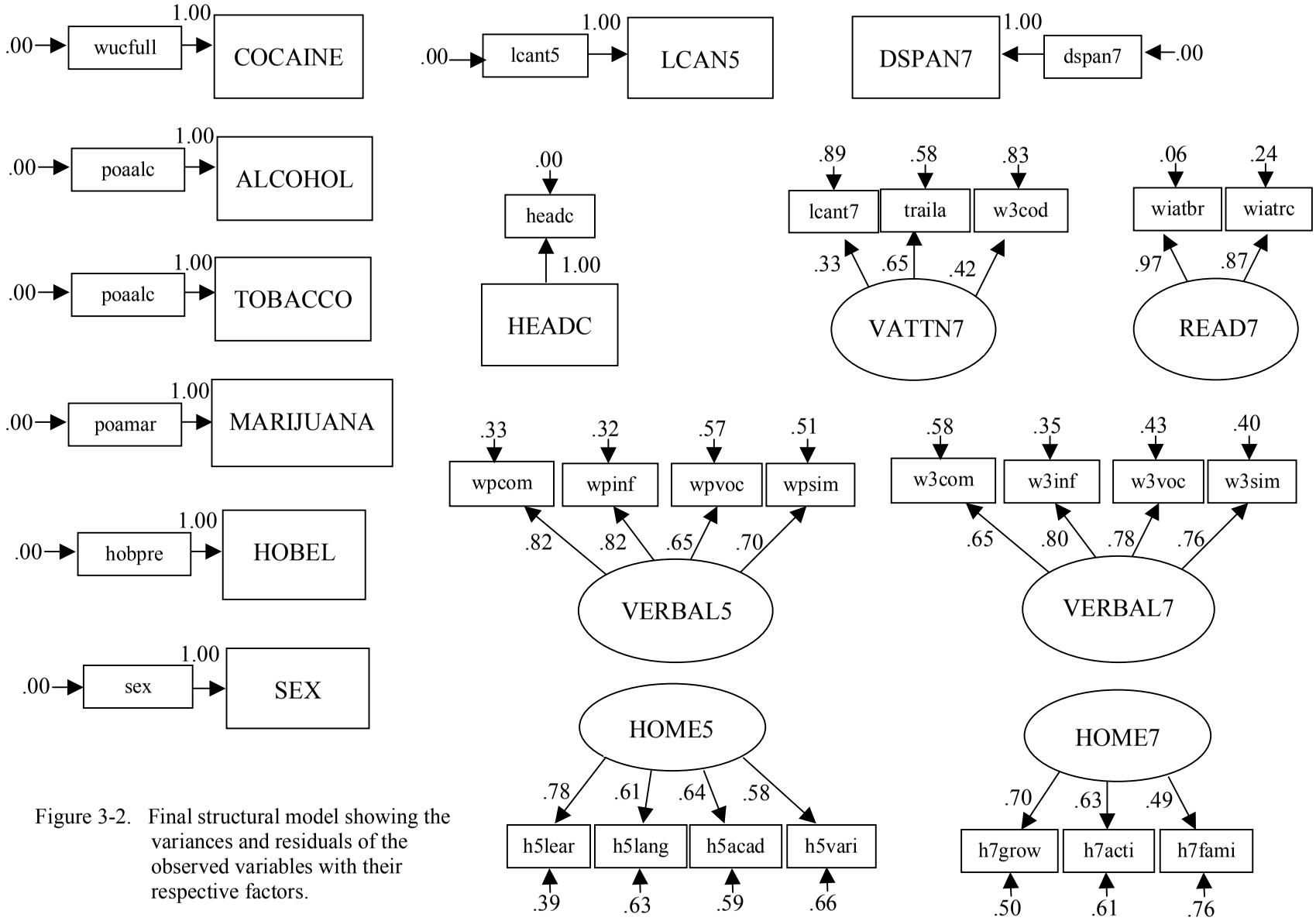

Figure 3-2. Final structural model showing the variances and residuals of the observed variables with their respective factors.

CHAPTER 4
DISCUSSION

Study Summary

In the current study, a group of children (*n* = 120) who were prenatally exposed to cocaine, alcohol, tobacco, and marijuana were compared to a matched group of children (*n* = 120) who were exposed to alcohol, tobacco, and marijuana but not cocaine. Statistical analyses showed that the group of children with prenatal cocaine exposure (PCE) had significantly higher levels of exposure to alcohol, tobacco, and marijuana and significantly higher prenatal obstetrical risk scores than their matched controls. The PCE group also had significantly shorter mean gestational age and mean head circumference at birth than the matched control group. The composition of the two groups did not differ significantly by ethnicity or sex. Both groups were predominantly African American and were almost equally split between boys and girls.

Main Findings

Three hypotheses were developed to examine the proposed relationships between prenatal cocaine exposure, attention, and reading ability. The first hypothesis, that measures of neonatal attention would be significantly related to measures of early childhood attention was not supported. With one exception, neonatal attention as measured by three scales of the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) was not significantly associated with a variety of attentional measures administered at ages 5 and 7, including a continuous performance test, short term auditory attention (Digit Span), or three attentional tasks involving visual scanning and

visuomotor coordination (Letter Cancellation, TMT Part A, and WISC-III Coding subtest).

The second hypothesis, that children with PCE would perform significantly worse than non-exposed children on measures of early childhood attention and reading ability was also not supported. No significant group differences were found on visual attention indices of a continuous performance test, short term auditory attention (Digit Span), or three visuomotor attentional tasks (Letter Cancellation, TMT Part A, and Coding).

Support was found, however, for the third hypothesis that PCE would have an indirect effect on reading ability that was mediated by head circumference and its subsequent effects of verbal ability and visual attention. Results of structural equation modeling on the combined sample of cocaine-exposed and nonexposed groups showed that PCE had a small negative effect on head circumference, with higher amounts of exposure associated with smaller head sizes at birth ($\beta = -.13$). Head circumference, in turn, predicted age 5 verbal ability ($\beta = .26$), which was highly predictive of age 7 verbal ability ($\beta = .93$). Age 5 verbal ability was also moderately related to two different age 7 attention factors, one comprised of Digit Span and the other by Letter Cancellation, TMT and Coding (βs = .52 and .47). Finally, the age 7 visual attention factor comprised of Letter Cancellation, TMT, and Coding was found to be the largest predictor age 7 reading ($\beta = .44$) followed closely by age 7 verbal ability ($\beta = .41$). Overall, the structural equation model accounted for 68% of the variance in age 7 reading ability.

Ancillary Findings

Between-group post hoc analyses revealed that the two study groups did not differ on verbal ability measures or 6 of 7 measures of the caregiving environment. The only

significant difference was found on the Growth Fostering Materials and Experiences subscale of the Middle Childhood Home Observation for Measurement of the Environment. Contrary to expectations, the difference favored the PCE group, probably because a much larger proportion of these children were in placements away from their biological mothers.

Several other findings from the structural equation modeling analysis also deserve comment. First, the small negative effect of PCE on head circumference ($\beta = -.13$) was very similar to that of prenatal exposure to alcohol and marijuana (βs = -.13 and -.11, respectively). Unexpectedly, prenatal tobacco exposure had a paradoxical effect on head circumference with higher levels of exposure associated with larger head sizes ($\beta = .14$). The similarity of the coefficients for the four drug exposure variables and the paradoxical positive coefficient for the tobacco exposure variable may be due to multicollinearity among these variables. An alternative approach would have been to combine the alcohol, marijuana, and tobacco exposure variables into a single "other drug exposure" variable. A decision was made not to follow this approach so that the potential effects of PCE could be compared directly with the effects of exposure to the other drugs measured in the study.

More than any of the drug variables, however, sex was the single strongest predictor of head circumference with girls having smaller heads at birth than boys ($\beta = -.22$). Sex also independently predicted the age 7 visual attention factor with girls outperforming boys ($\beta = .29$). None of the drug variables nor head circumference were direct predictors of the age 5 or age 7 attention factors.

Study Findings in the Context of the Literature

Hypothesis #1. That the three BNBAS scores used in the current study were not predictive of early childhood attention measures is not wholly surprising. First, the majority of studies that have assessed the predictive validity of infant attention for later cognitive abilities have not utilized the BNBAS. Most studies have employed experimental habituation paradigms that are not widely used in the clinical assessment of infants. Thus, while useful as a broad-based clinical tool for assessing the adaptation of infants to their extrauterine environment, the BNBAS and its specific cluster scores may not have the sensitivity or specificity needed for research applications.

Second, the BNBAS has typically been used to predict general cognitive abilities, such as IQ or language development, rather than attention in particular. While there are a handful of studies that have begun to trace the developmental trajectory of attention from infancy to childhood, none have used the BNBAS. For the studies reviewed in Chapter 1, two experimental paradigms, fixation duration and exposure time needed to meet criterion during a visual recognition memory task, were the measures used to predict later attentional abilities, respectively (Sigman et al., 1991, Rose & Feldman, 1995). Thus, the attempt in the current study to predict childhood attentional performance using the BNBAS was a venture into relatively unchartered territory.

Third, studies comparing infant and early childhood performance on attentional or other cognitive tasks generally do not use neonates. In the review by Colombo (1993), the age at the first assessment ranged from 3 to 9 months. The reason may be that scores based on assessments of newborns using measures such as the BNBAS are likely to reflect the state of the child at the time of the assessment rather than a more enduring trait that is not expected to change significantly over time. Using the BNBAS in newborns,

then, is somewhat akin to using a state measure to predict a childhood trait (attention). Such an undertaking is less likely to produce significant results, especially considering that attention is not a stable attribute in childhood but continues to develop with age (Cooley & Morris, 1990).

Finally, the hypothesis that BNBAS scores would be predictive of later attentional measures was based, in part, on group differences on the BNBAS reported in the literature between children with PCE and non-exposed children. A meta-analysis of group differences on the BNBAS between children with PCE and non-exposed children has revealed that the largest reliable differences were for motor performance and abnormal reflexes and not for the Orientation, Habituation, or Regulation of State scores (Held, Riggs, & Dorman, 1999). It was also found that while the Orientation and Autonomic Regulation clusters produced small, significant effects at birth and at 3 to 4 weeks of age, the effects were small, decreased over time, and were likely due to a large sample size (Held, Riggs, & Dorman, 1999). Thus, attentional differences found between infants with PCE and comparison groups in some studies did not hold up across samples. In sum, considering the lack of reliable between-group differences on the BNBAS for cocaine-exposed and non-exposed children, combined with the three BNBAS measurement issues just outlined, it would have been quite remarkable if the three BNBAS scores used in the present study were significantly correlated with attention measures at age 5 and 7.

Hypothesis #2. The lack of significant group differences on attention and reading measures between children with PCE and non-exposed children in the current study is consistent with the majority of the literature in this area. In a recent review, Frank,

Augustyn, Knight, Pell, and Zuckerman (2001) concluded that after controlling for confounding factors, PCE has no consistent negative association with physical growth, developmental test scores, or language skills. However, it should be noted that the majority of studies included in the review examined outcomes for children age 3 or younger. Only two other groups of researchers have published data on children with PCE over age 3 using assessment instruments similar to those in the current study. Hurt et al. (1997) found no group differences at age 4 between a Philadelphia inner-city sample of children with PCE and non-exposed children on the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) mean Verbal, Performance, or Full Scale IQ scores. Richardson, Conroy, and Day (1996), based in Pittsburgh, found no group differences at age 6 between children with PCE and non-exposed children for any scores on the Stanford-Binet Intelligence Scale-Fourth Edition (Thorndike, Hagen, & Sattler, 1986) or on the Reading, Spelling, or Arithmetic subtests of the Wide Range Achievement Test-Revised (Jastak & Wilkinson, 1984). As in the current study, the Pittsburgh research team found that both groups of children generally scored in the average range on IQ and achievement measures (Richardson et al., 1996).

Three published studies of attentional abilities of school-age children with PCE and non-exposed children were found in the extant literature. The first two, from the same group of researchers (Richardson et al., 1996; Leech et al., 1999). In the first study, the authors compared exposed and non-exposed groups the using a continuous performance task (CPT) involving shapes and colors that is not widely available for commercial use. In their sample, the 6-year-olds with PCE made significantly more errors of omission across all three blocks of trials than did non-exposed children; however, no

group differences were found for errors of commission (Richardson et al., 1996). It was later reported that among those excluded from the analyses were 13 children who did not complete the test to due "impulse control and attention problems" and an unspecified number of children refused to do the task (Leech et al., 1999). The proportion of these children who had PCE and their characteristics are not reported. In a follow-up study, the authors found that PCE during first trimester predicted more errors of omission; however, marijuana use during second trimester and tobacco use during the second and third trimesters were also predictive of more errors of omission (Leech et al., 1999). For all drug exposure variables, the regression coefficients were small ranging from .09 to .10, raising the question about whether these effects are meaningful in terms of the everyday functioning (e.g., school performance) of children with PCE.

In the third study, Bandstra, Morrow, Anthony, Accornero, and Fried (2001) conducted a longitudinal investigation of attention in school-age children with PCE using two different CPT tasks. They used the Test of Variables of Attention (TOVA; Greenberg et al., 1996) at age 5 and the Conners' Continuous Performance Test (CCPT; Conners, 1995) at age 7. Using omission errors as the criterion variable, they found that age 5 scores predicted age 7 scores. While the noncocaine-exposed control group performed better on both measures than the children with PCE, between-groups statistical analyses were not conducted to determine whether the differences were significant. A between groups analysis, combining the two CPT measures with an age 3 "time on task" measure of attention, revealed that the estimated group difference was significant. Hierarchical models that included birth outcome measures such as head circumference did not significantly attenuate the between-groups difference. Using SEM, the authors also found

that the amount of PCE significantly predicted omission error scores at age 7 even after controlling for other prenatal drug exposure, child's age, and child's sex ($\beta = .26$) (Bandstra et al., 2001).

The current study found no differences between children with PCE and non-exposed children for two indices of visual attention on the Intermediate Visual and Auditory Continuous Performance Test (IVA CPT). Between-group differences on errors of omission and errors of commission were not examined but such data are available for the sample used in the current study and could be the focus of a future study.

Hypothesis #3 -- Relationship between PCE and head circumference. The finding that the relationship between PCE and cognitive variables is mediated, in part, by head circumference is consistent with the published literature. Currently, only four other studies have examined the relationships between PCE, head circumference, and developmental outcomes. Two of these studies focused on 24-month outcomes, and two studies examined 36-month outcomes. In the first study, Chasnoff et al. (1992) found significant correlations between head circumference at various ages up to 24 months and Mental and Psychomotor indices of the Bayley Scales of Infant Development (Bayley, 1969). While prenatal exposure to cocaine, alcohol, tobacco, and marijuana all contributed to head circumference measurements during the first 2 years, only cocaine was a significant predictor as a single variable in their Chicago-based sample (Chasnoff et al., 1992).

Another group of researchers found that head circumference at birth is correlated with BSID scores at 6.5, 12, and 24 months of age in a mixed sample of cocaine-exposed and non-exposed children ($N = 415$) (Singer et al., 2002). Significant correlation

coefficients between head circumference and BSID Index scores ranged from .12 to .22 (Singer et al., 2002). Using stepwise regression to develop a model predicting scores at 24 months, it was found that the negative effects of cocaine on cognitive outcome were mediated through smaller head circumference at birth (Singer et al., 2002). No other measures—gestational age, birth weight, birth length, Apgar scores, or the Hobel Neonatal Risk score—mediated the effects of cocaine on BSID scores obtained at 24 months (Singer et al., 2002).

In the third study, Azuma and Chasnoff (1993) used path analysis to determine whether head circumference was a significant predictor of age 3 developmental outcome assessed using the Stanford-Binet Intelligence Scale-Fourth Edition (SBIS; Thorndike, Hagen, & Sattler, 1986). While head circumference at age 3 was not found to be a direct predictor of the SBIS composite IQ score at age 3, it did have an indirect effect on composite IQ that was mediated by poor perseverance as measured by a combination of five-point behavior rating scales completed by the blinded examiners who administered the SBIS (Azuma & Chasnoff, 1993). The regression coefficients were -.30 between head circumference and perseverance and -.60 between perseverance and composite IQ (Azuma & Chasnoff, 1993).

The fourth study to examine head circumference as a predictor variable was conducted by principal investigators of the grant from which the sample for current study was drawn. Using structural equation modeling, it was found that age 3 developmental outcome measured by a factor comprised of BSID scores and four subtests of the Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984) was predicted by birth head circumference ($\beta = .14$), which itself was predicted by prenatal

cocaine exposure ($\beta = -.18$) after controlling for prenatal alcohol and tobacco exposure (Eyler, Behnke, Garvan, Wobie, & Hou, 2002). While interpretation is made somewhat more difficult by the study's use of an outcome variable that combined scores from both a child behavioral measure (BSID) and a caregiver report measure (VABS), it is clear that head circumference was a mediator between PCE and overall developmental outcome.

The results of the current study and the four studies just reviewed suggest that head circumference may serve as a proxy for the effects of PCE on in utero brain development. While three different groups of researchers have found significant relationships between head circumference and BSID scores, these studies do not elucidate the mechanism underlying the relationship. In the Azuma and Chasnoff (1993) study, however, perseverance was the factor linking head circumference to Stanford-Binet composite IQ. In the current study, head circumference predicted verbal ability, verbal ability predicted visual attention, and visual attention was found to be the most significant predictor of reading performance. If sustained effort (perseverance) is considered somewhat analogous to sustained attention, then the results of the Azuma and Chasnoff (1993) study and the current study arguably converge to suggest that PCE's effect on head circumference may be related to problems with self-regulation that can affect cognitive performance. These findings warrant further studies using head circumference, particularly at birth, as a predictor variable in future studies of developmental outcomes of children with PCE.

Hypothesis #3 - Relationship Between Attention and Reading. While there are no current published studies on the relationship between attention and reading in children with PCE, the finding that attention is strongly related to reading ability is consistent with

other longitudinal studies using samples of elementary school children. Using path analysis, Rabiner, Coie, and The Conduct Problems Prevention Research Group (2000) found that teacher ratings of inattentiveness in second grade had a regression coefficient of -.10 with fifth-grade reading achievement in a combined sample of both "at-risk" and "normal" children. Using structural equation modeling and a much larger sample of children drawn from the normal school population, Rowe and Rowe (1992) found that teacher ratings of inattentiveness had a strong negative influence across four age groups with regression coefficients ranging from -.21 to -.39. The much larger regression coefficients in the current study may be the result of using direct behavioral measures of attention rather than teacher ratings.

Overall, the results of the current study suggest that the effects of PCE, if any, on school-age outcomes such as attention and reading are subtle and difficult to detect using traditional pencil and paper assessment methods. The effects of PCE that can be identified are of similar magnitude as those associated with prenatal exposure to alcohol and tobacco, which are used by pregnant women more often and in larger quantities. Distinguishing the effects of prenatal drug exposure on later childhood development is complicated by the fact that children born to mothers who abused substances during pregnancy are subject to other multiple risk factors for poor outcome, including poverty. Studies on children with PCE, including the current one, seem to point to the resiliency of humans to develop normally despite multiple risk factors rather than the strength of the teratogenic model to predict negative outcomes.

Study Strengths

The strengths of the current study result from the nature of the sample, control for potentially confounding variables, and the use of structural equation modeling. The

sample is distinguished from that of other prospective, longitudinal studies in that examiners were blinded to the children's cocaine exposure status and the attrition rate was very low (approximately 10%). In the Frank et al. (2001) review, the authors excluded 20 studies because they failed to guard against examiner bias by masking the cocaine exposure status of the children. The distortions that can result from examiner bias, particularly in behavioral research, are well-known (Kazdin, 1980). Moreover, researchers have documented specific negative examiner bias with children labeled as prenatally exposed to cocaine (Thurman, Brobeil, & Ducette; 1994; Woods, Eyler, Conlon, Behnke, & Wobie, 1998). Obtaining data from blinded examiners has not been a universal feature of studies of children with PCE and makes the results of the current study more trustworthy.

Careful analysis of the characteristics of the sample and how it compares to the originally enrolled sample is another important feature of the current study. For the studies included in the Frank et al. (2001) review, retention rates ranged from 39% to 94%, characteristics of those lost to follow-up were not reported for 6 of the 17 independent cohorts, and four studies failed to report attrition at all (Frank et al., 2001). A wide variety of factors can affect which participants remain in longitudinal studies, including the severity of the problems being studied. Thus, in order to ascertain the potential longer-term effects of any variable, it is critical to understand the nature of the sample and how it changes over time. The sample in the current study represented 78% of the original sample, including the children who died, and replicated the original group differences in prenatal drug exposure, Hobel prenatal risk, and birth head circumference. The current study groups were also similar to the original study groups in that they did

not differ in terms of ethnicity or sex. The one statistically significant difference between the current study groups that was not found in the original study groups—gestational age—was less than one week and did not represent a significant clinical difference.

A third strength of the current study is control for, and comparison of, confounding variables. Failure to control for confounding variables, particularly exposure to other drugs of abuse, is one of the most prevalent methodological flaws in the literature on children with PCE. The original study groups were matched for demographic variables including ethnicity, and the demographic similarities between the groups were maintained in the current study sample, thereby controlling for these variables. Using separate factors for prenatal exposure to cocaine, alcohol, tobacco, and marijuana in the structural equation model allowed direct comparison of the relative effect of each drug. These direct comparisons are important because they help to contextualize the effects of PCE in terms of alcohol and tobacco—drugs that are more familiar to health professionals and the public and are more commonly used by pregnant women. Considering that women who use cocaine during their pregnancies are, in some states, currently subject to punitive consequences (while women who use alcohol and tobacco are not), the ability to make comparisons between various drugs of abuse could have important policy implications.

The use of structural equation modeling is not yet common in research on children with PCE and represents a significant contribution to the literature. Structural equation modeling is a powerful statistical technique that enables researchers to pose and test hypotheses that cannot easily be evaluated using more traditional statistical methods. In the current study, no statistically significant differences were found between children

with PCE and non-exposed children in a cross-sectional analysis using traditional statistical techniques. However, the relationship between attention and reading and between PCE and attention could still be explored using structural equation modeling.

Study Limitations

Measurement issues. One of the primary limitations of the current study relates to the methods used to measure attention. Attention is a complex, multi-dimensional process that involves a number of distinct areas of the brain, depending on the nature of the task. In the current study attention was measured using one auditory task and three pencil and paper tasks: Digit Span, Letter Cancellation, TMT Part A, and Coding. Since the Digit Span factor did not turn out to be a significant predictor of reading, this discussion will focus on the latter three tasks.

Letter Cancellation, TMT Part A, and Coding were combined into a factor labeled "visual attention;" however, each of these tasks require much more than "attention" to be completed skillfully and efficiently. All three tasks involve visual scanning, have a significant fine motor component, and require familiarity with letters or numbers or both. Moreover, all three tasks are timed, and scores are based primarily on speed with a secondary emphasis on accuracy. Arguably, then, the factor comprised of these tasks could have been called a "processing speed" measure rather than an "attention" measure. Additionally, it should be noted that there was some variability in how the children performed on each of the tests. While both groups of children scored in the average range on Coding, mean scores for TMT Part A for both groups of children were more than 1.5 standard deviations below published norms. This highlights the fact that these tests may tap different aspects of the multidimensional construct called attention.

Generalizability issues. The participants in the current study were drawn from rural north central Florida. By contrast, the majority of the prospective longitudinal studies on the effects of PCE funded by the National Institute on Drug Abuse are based in large urban centers, namely Atlanta, Baltimore, Chicago, Cleveland, Detroit, Miami, and Pittsburgh. This significant geographical difference could affect a variety of factors that impact child developmental outcome, ranging from the amount and quality of drugs used by the mothers to the amount and quality of social supports available to mothers and intervention programs available to the children. Although the overwhelming majority of the participant families in the NIDA-funded studies are poor, poverty is likely to be experienced quite differently in a rural area than in an urban area. The potential impact that a rural versus an urban setting may have on developmental outcomes of children with PCE remains an empirical question that warrants further research.

Future Directions

Several of the suggestions for helping to elucidate the relationships found between PCE, attention, and reading in the current study relate to measurement issues. First, no significant relationship was found between the Digit Span factor and the Reading factor, and this may be due to the fact that scaled scores that combine performance on Digits Forward and Digits Backward were used. Digits Forward is traditionally considered an attentional task, while Digits Backward, which requires manipulating the information presented, is considered a working memory task and more difficult than Digits Forward. Two children could obtain identical scaled scores on the combined Digit Span task, with considerably different performances on Digits Forward vs. Digits Backward. Thus, using raw scores for Digits Forward and Digits Backward

may have revealed significant between-group differences or resulted in significant predictive relationships between Digits Forward or Digits Backward and reading ability.

Second, as discussed earlier, the Visual Attention factor was comprised of three tasks that involved both visual scanning and visuomotor processing speed. To assess the relative importance of these two sets of component skills to reading ability, a task that relies primarily on motor speed, such as the Finger Tapping Test from the Halstead-Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1985) or mean reaction time on the IVA CPT (Sandford, 1995), could have been used as a covariate in the analyses. Although no consistent negative effects of PCE have been found for motor development (Frank et al., 2001; Singer et al, 2002), analysis of scores on motor and visual-motor tasks could help to clarify the variability in performance across the different measures of visual attention and how they may affect reading skills.

Third, future studies should examine single-word reading skills separately from reading comprehension. In the current study, the Reading factor was comprised of two subtests, Basic Reading and Reading Comprehension, that assess different aspects of reading ability. The Basic Reading subtest is largely a measure of single-word reading and relies on sight word recognition for familiar words and phonological decoding skills for unfamiliar words. The other subtest, Reading Comprehension, involves reading short passages and answering questions posed by the examiner. It may be that the visual scanning aspects of the Visual Attention factor, comprised of Coding, Letter Cancellation, and TMT Part A, may be more related to single word reading while the working memory aspects of the Digit Span factor and the general information knowledge and vocabulary skills captured in the Verbal Ability factor would be more associated with

reading comprehension, which requires higher order synthesis of material as it is read. In short, more detailed analysis of which aspects of attention map onto which aspects of reading could be the focus of future studies.

Fourth, it is likely that there are subgroups among the children with PCE who differ in ways that may affect outcome. For example, there was some variability in the amount and timing of cocaine exposure among the children with PCE. By combining children with low- and high-exposure or children with predominantly first-trimester versus third-trimester exposure in the analyses, significant subgroups differences may have been diluted or even eliminated. Another example of potentially important subgroup differences has to do with exposure to multiple teratogens. At least one animal study has reported that maternal use of alcohol and cocaine during pregnancy has more detrimental effects on offspring outcome than use of either drug alone (Randall, Cook, Thomas, & White, 1999). Since human maternal cocaine use during pregnancy most often occurs in conjunction with other drugs of abuse, studies of the coteratology of cocaine with alcohol, tobacco, and marijuana should become the research wave of the future.

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BIOGRAPHICAL SKETCH

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