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Longitudinal Effects of Family Variables and Illness Severity on Cognitive Functioning in Children with HIV Infection

Heather Jordon Clark
Georgia State University

LONGITUDINAL EFFECTS OF FAMILY VARIABLES AND ILLNESS SEVERITY ON COGNITIVE FUNCTIONING IN CHILDREN WITH HIV INFECTION

By

HEATHER JORDON CLARK

Under the Direction of Lisa Armistead and Pamela Bachanas

ABSTRACT

Although HIV/AIDS is the 9th leading cause of death in African-American children, 80% of HIV-infected children in the U.S. live into school-age years. This study focuses on associations between HIV illness severity, family factors, and long-term cognitive functioning of these children. Participants included 42 perinatally HIV-infected children (mean age = 72.4 months), 93% of whom were African-American. Mean intellectual functioning was more than one standard deviation below the normative mean; whereas, overall language and attention functioning were generally not different from the normative sample. First, this study described changes in functioning over time and/or between genders. Analyses of variance were conducted for five outcome variables (i.e., full scale IQ, verbal IQ, performance IQ, expressive and receptive one word picture vocabulary test). Expressive language scores increased over time. For receptive language, males' skills improved significantly over time, while the decline in females' skills did not reach significance. Second, the associations between Time Two illness severity (i.e., viral load), and Time One familial variables (i.e., adult-to-child ratio in the home, number of caregivers lost to death, number of months since caregiver death), with outcome

variables at Time Two (i.e., intellectual, language, and attentional/hyperactivity functioning) were examined. For intellectual and expressive language, only the respective Time One functioning independently contributed a significant amount to Time Two functioning. For receptive language, Time One receptive language and the adult-to-child ratio in the home significantly predicted Time Two functioning. As the number of adults per child increased, there was an improvement in receptive language functioning. For both measures of language, the interaction between Time Two illness severity and Time One months since caregiver death significantly predicted Time Two functioning. With no loss of caregiver, more ill children demonstrated better language abilities than less ill children. Across illness groups, children performed similarly after a recent caregiver death. With greater time since caregiver death, the less ill children performed better than their more ill peers. For attention/hyperactivity, no predictor variables were significant. Interventions that consider family factors, as well as medical information, as potential influences on future child functioning may aid in the battle against this chronic illness.

INDEX WORDS: HIV, Children, Cognitive functioning, Family, Longitudinal

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HEATHER JORDON CLARK

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HEATHER JORDON CLARK

Major Professor:	Lisa Armistead
Committee:	Pamela Bachanas
	Sarah Cook
	Mary Morris

Electronic Version Approved:

Office of Graduate Studies
College of Arts and Sciences
Georgia State University
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CHAPTER 1: INTRODUCTION

Since the first case of pediatric AIDS was described in 1982 (Ammann, 1994), the Centers for Disease Control and Prevention (CDC) has estimated there are a total of 9,419 pediatric AIDS cases (children < 13 years old) and an additional 4,579 pediatric HIV cases (CDC, 2004) in the United States. Over 58% of children diagnosed with AIDS have died (CDC, 2004); making HIV/AIDS the 13th leading cause of death in U.S. children (5-14 years old) (CDC, 2005). The CDC reports that there were approximately 2,614 U.S. children (<13 years old) living with HIV/AIDS at the end of 2003 (from areas with confidential HIV infection reporting). Fortunately, the estimated number of new pediatric AIDS cases in the U.S. has fallen from 954 in 1992 to 59 in 2003 (CDC, 2004), due largely to prenatal care and medication for HIV-infected pregnant women.

In 2002, the CDC found that an increasing proportion of people with AIDS are African-American or Hispanic, female, residents of the South, and exposed to HIV through heterosexual contact (MMWR, 2002). Thus, African-American children are disproportionately represented among pediatric AIDS cases in the United States, constituting 59% of all reported cases through 2003 (CDC, 2004), yet they are only 15.5% of U.S. population of children (US Census Bureau, 2004). Among African-American children across the U.S., HIV/AIDS is currently the 9th leading cause of death (CDC, 2005).

Though some HIV-infected children die within the first two years of life, recent medical advances have resulted in 80% of U.S. children with HIV infection living past five years of age (hivpositive.com/index.html). Unfortunately, the majority of these children experience

numerous hardships associated with the course of their illness. Research indicates that HIV affects the psychosocial, behavioral, cognitive, motor, and language functioning of infected children. Additionally, home environment and family variables have been implicated as having an influence on the functioning of HIV-infected children (e.g., cognitive performance; Boivin et al., 1995; Coscia et al., 2001; Kullgren et al., 2004). For example, most children who are HIV-infected acquire the illness perinatally via maternal infection. Thus, children in these families may experience the death or progressive illness of their mother. Maternal illness may compromise parenting (Kotchick, Brody, Forehand, Armistead, Simon, Morse, & Clark, 1997), which, in turn, can negatively affect child functioning. The combination of illness factors and compromised family functioning often present in the homes of infected children make it important to gain a better understanding of the roles of illness severity and family factors with respect to infected children's cognitive functioning. Descriptive analyses, in the present study, will provide information about the extent to which functioning changes over time and/or differs across gender. The present investigation also examines whether cognitive functioning differs as a function of illness severity and family variables longitudinally. Furthermore, possible interaction effects of illness severity and family variables on cognitive functioning will be considered.

Effects of HIV on Cognitive Functioning

Although pediatric HIV has historically received less attention than adult HIV, many notable findings have emerged over the past 10-15 years. Psychologists and neurologists have worked in concert to increase understanding of how disease and environmental variables influence various domains of functioning. Three areas of cognitive functioning that have received attention are intellectual abilities, language skills, and attentional/hyperactivity

difficulties. Findings germane to the latter three areas hail from literature addressing differences in functioning between HIV-infected and non-infected youth; the relationship between biological markers of illness severity and functioning in HIV-infected children; and the few longitudinal studies that have been conducted.

Intellectual functioning. In the present study, intellectual functioning is defined as a child's intelligence quotient as measured by a standardized test (i.e., WPPSI-R [Wechsler, 1989]; WISC-III [Wechsler, 1991]). Comparative findings of intellectual functioning between HIV-infected and non-infected children or the norming sample for particular measures will be reviewed first. Next, findings about the influence of HIV illness severity (e.g. viral load) on intellectual functioning will be presented. The discussion will close with longitudinal findings regarding the intellectual functioning of HIV-infected children.

Studies comparing HIV-infected and non-infected children are inconsistent with regard to intellectual functioning. Researchers have compared the performance of HIV-infected and non-infected children, or relevant published norms, across a range of areas with some observing differences. For example, Nozyce and colleagues (1994) found significant cognitive deficits in symptomatic HIV-positive children, as compared to seroreverter and non-HIV-infected control children. However, *symptom-free* HIV-positive children showed no difference in functioning relative to matched non-infected children in the Nozyce study. Blanchette and colleagues (2001) reported impairments in mental development (using the mental scale of the Bayley Scales of Infant Development) in HIV-infected, but not non-infected, children born to HIV-positive mothers. Lastly, Papola et al. (1994) reported that 56% of a sample of 90 vertically infected children were functioning at a borderline or lower level of intelligence, and Kullgren et al.

(2004) found that the average scores of a sample of HIV-infected children fell below the normative sample on measures of IQ.

In contrast to those studies demonstrating differences on intellectual measures for HIV-infected versus non-infected children, other researchers have not found differences. Cohen and colleagues (1991) compared HIV-negative and HIV-positive children on measures of adaptive functioning at home and school. Across groups, there was no significant difference in intellectual functioning. Tardieu and colleagues (1995) found similar results in that 2/3 of their HIV-positive sample had normal school achievement, with a mean IQ in the normal range. However, it is important to note that the Tardieu sample only consisted of 6-year-olds and thus, did not include children who suffered severe AIDS-related illness and who had died by age six. The literature is further complicated by the fact that some researchers did not find global differences in intelligence but did see focal deficits (e.g., executive functioning) when comparing infected and non-infected children (e.g., Bisiacchi et al., 2000; Fishkin et al., 2000). In summary, while some researchers observed differences in intellectual functioning between HIV-infected children and those who are not (or the relevant norming groups), others have not observed these differences, or observed them in select areas. Differences appear to be related, at least in part, to the severity of the HIV illness (e.g., Nozyce et al., 1994). Furthermore, Blanchette et al. (2002) have regarded the inconsistencies within and across studies as plausible evidence that factors other than HIV (e.g., environmental factors) may be contributing to child outcomes.

While studies comparing HIV-infected to non-infected children or their norms are less consistent, most cross-sectional studies examining only HIV-infected children appear to demonstrate a relationship between disease severity and intellectual functioning. Specifically,

several cross-sectional studies have demonstrated an association between immune system integrity and cognitive functioning (e.g., Brouwers et al., 1995; Henry et al., 1996; Pollack et al., 1996). For example, among a sample of HIV-infected children, HIV viral load (the amount of circulating virus), particularly within the first few months of life, was correlated with cognitive development. As viral load increased, achievement of cognitive milestones was more delayed (Pollack et al., 1996 as cited in Wachsler-Felter & Golden 2002). Additionally, Nozyce and colleagues found that mental impairments were more evident when HIV-positive infants developed a serious AIDS defining illness within the first two years of life, than if they did not (Nozyce et al., 1994). However, using a sample that significantly overlaps with the present study sample, Kullgren et al. (2004) found that although HIV-infected children scored, on average, below national norms, illness variables (i.e., CD4 count) did not contribute significantly to the prediction of cognitive functioning. Perhaps the variation in the markers used for disease severity partially explains these differences. Studies using viral load and the presence of illness found IQ differences, while the study using CD4 count did not. In summary, with the exception of Kullgren et al. (2004), these studies offer some evidence that more severe illness forecasts intellectual impairment.

Two longitudinal studies have also focused on the intellectual functioning of HIV-infected children and adolescents. The first study, Loveland et al. (2000), demonstrated a direct relationship between declining immune functioning and declining neuropsychological functioning in HIV-positive children, adolescents, and young adults with hemophilia over time. Significant declines over time and across illness groups were found in nonverbal intelligence, perceptual/performance skills, nonverbal memory, academic achievement, and language. In contrast, Wolters et al. (1997) found no change in overall cognitive functioning (i.e., FSIQ) of 1-

to 13-year-old HIV-infected children over a 24-month period, despite treatment with antiretroviral medication. Furthermore, there was not a significant difference in FSIQ between children who were previously treated and untreated with antiretroviral therapy. In summary, many studies indicate that HIV is associated with compromised intellectual functioning among children, and the more recent literature points to the importance of examining subcomponents of overall intellectual functioning (e.g., Bisiacchi et al., 2000; Fishkin et al., 2000). Moreover, illness severity as measured by viral load or an AIDS defining illness, appears to magnify the discrepancy in intellectual functioning between infected and non-infected children. However, it is important to note that the intellectual functioning of HIV-infected children may also be compromised by non-illness related factors.

Language functioning. Similar to the review of intellectual functioning, studies comparing HIV-infected to non-infected children are presented first, followed by a discussion of language functioning as it relates to HIV illness severity, and ending with longitudinal studies of HIV-infected children. As with the domain of intellectual functioning, studies comparing language functioning of non-infected controls to HIV-infected children have produced mixed findings. For example, Wolters and colleagues (1995) found that non-infected siblings exhibited better language skills than their HIV-infected siblings, with better-developed receptive language than expressive language. However, Bisiacchi et al. (2000) reported normal language abilities for HIV-infected and non-infected neurologically asymptomatic children. Furthermore, Havens and colleagues (1993) reported that children with HIV did not differ from seroreverted and control children on measures of language abilities. Again, these discrepant findings may be indicative of factors other than HIV contributing to outcomes.

With regard to illness severity, Nichols et al. (2000) demonstrated that poorer adaptive functioning, particularly in the communication domain, was associated with advancing immuno-compromise. Similarly, Wolters et al. (1995) found that children with more compromised immune systems exhibited more impaired language functioning. With respect to expressive and receptive language, several studies suggest that expressive skills are more profoundly damaged than receptive language skills in children with advanced HIV disease (Condini et al., 1991; Pressman, 1992; Wolters, 1992; Wolters, Brouwers, Moss, & Pizzo, 1994). Additionally, African-American children may be particularly compromised as Llorente and colleagues (2004) found that African-American children's scores were significantly lower than European American children on the Expressive One-Word Picture Vocabulary Test-Revised, even after controlling for immunologic clinical category and CD4+ percentage. In sum, most evidence suggests that expressive and receptive language skills are impaired, particularly among symptomatic and African-American children, with expressive skills being more adversely affected than receptive skills.

What little longitudinal data there are, suggest that disease progression is associated with impairment in language functioning (Tardieu et al., 1995). Specifically, children with low CD4 levels (a marker of the immune system's integrity) during the first years of life were at higher risk for later school problems, relative to children with better immune functioning. Wolters et al. (1997) reported that expressive language was consistently more impaired, and both receptive and expressive language functioning declined significantly after 24 months, despite antiretroviral therapy. These results indicate that advancing immunocompromise is associated with poorer communication skills, particularly expressive language. Taken together, these findings suggest

that a longitudinal design is needed with further exploration of possible influences, in addition to illness severity, on language functioning.

Attention/hyperactivity difficulties. Finally, I review the literature as it relates to attention/hyperactivity difficulties, beginning with those studies that compare HIV-infected children to non-infected children and ending with studies that consider illness severity. No longitudinal studies examining attention problems and HIV could be located in the literature.

There has been less research examining behavioral disorders in children with HIV, relative to intellectual and language functioning. One study reported "hyperactivity disturbance" in 34% of a sample of HIV-infected children (Corsi et al., 1991), and another reported severe attentional deficits in 53% of an HIV-infected sample greater than four years old (Hittleman et al., 1993). Several researchers have also reported attentional weaknesses or deficits in children with HIV on measures that are partly dependent on attentional skills (e.g., WISC-R Freedom from Distractibility factor [Kaufman, 1975]; K-ABC Hand Movements, Number Recall, and Spatial Memory subtests) (Boivin et al., 1995; Brouwers et al., 1989; Brouwers et al., 1992; Cohen, 1991; Hittleman et al., 1993). Moreover, Kullgren et al. (2004) found that HIV-infected children had significantly more problems than the normative sample in several areas of behavioral functioning (as measured by the Conners' Parent Rating Scale).

Thus, while several researchers have observed more attention/hyperactivity-related behavioral problems for HIV-infected children, others have not, indicating the importance of factors other than those directly attributable to the illness. For example, among a group of 5- to 12-year-old HIV-infected children, 58% exhibited attention-deficit/hyperactivity disorder; however, HIV-infected children were no more likely than control (non-HIV-exposed) and seroreverter children to receive this diagnosis (Havens et al., 1993). In another sample, teacher

and parent ratings of attention/hyperactivity were not significantly different for HIV-infected versus non-infected children (Cohen et al., 1991). Furthermore, children with HIV have been shown to have comparable attention skills to children with hemophilia (but not HIV) (Whitt et al., 1993) and children with acute lymphoblastic leukemia (Brouwers, Moss, & Poplack, 1992). Perhaps the discrepancy can be explained in part by the breadth of the measurement tools utilized. It appears that while HIV-infected children show focal areas of attention or hyperactivity weakness; they are not differentiated from non-infected groups with regard to global indicators of attention/hyperactivity disorders.

With greater illness severity, more brain damage is typically present, which likely compromises attentional skills in HIV-infected children (Llorente, LoPresti, & Satz, 1997). However, Moss et al. (1994) found no attentional differences between encephalopathic and nonencephalopathic children, and no significant effect of antiretroviral therapy on a Q-sort procedure. Moss concluded that it is likely that factors other than physiological ones are influencing the attentional functioning of HIV-infected children.

In summary, the extant literature is equivocal with respect to whether HIV-infected children are comparable to their non-infected peers in terms of instance and intensity of global attention and hyperactive problems. The factors that contribute to attentional deficits in HIV-positive children remain unclear, but impairments may be more focal than global in scope. Moreover, environmental factors need to be examined further regarding their unique contributions to attentional deficits and hyperactivity observed in children with HIV.

Many, though not all, studies support the premise that HIV affects cognitive (i.e., intellectual, language, and attention/hyperactivity) functioning. An earlier cross-sectional study (Kullgren et al., 2004), which utilized children from the same clinic as the current study,

concluded that HIV-infected children performed below the normative sample on IQ and above normative samples (which represents more problematic behavior) on specific behavior scales. The present study sought first to expand this research by examining cognitive functioning across two points in time, separated by no more than 36 months. Second, as suggested by more recent findings (Bisiacchi et al., 2000; Fishkin et al., 2000; Wachsler-Felder & Golden, 2002) and demonstrated in Kullgren's work (2004), multiple measures of intellectual functioning were used (i.e., Full Scale IQ, Verbal IQ, Performance IQ) to allow for identification of more specific differences between groups within the area of intellectual functioning. Third, early HIV studies were conducted on very few participants (Rosner et al., 1985 N=9; Scott et al., 1984 N=14), while this study included approximately 40 HIV-infected participants. Given the previous literature review, there is an evident need for longitudinal studies examining cognitive functioning among HIV-infected children. The author speculates that these investigations may be influenced by illness progression, as well as advances in anti-HIV medications. This study also contributes to the literature by expanding knowledge in the field of pediatric HIV through conducting gender comparisons, which are not often found regarding cognitive functioning. The current study will examine the effect of gender on intellectual, language, and attention/hyperactivity.

Effects of Family Variables on Cognitive Functioning

Until recently, literature in this area was largely void of any recognition of the role of familial and environmental variables in functioning of children with HIV. Yet, the effects of HIV in a child likely extend beyond the biology of the illness. Thus, the influences of two factors of the child's home environment were considered in this study. Studies with healthy children indicated that home environment accounts for some of the variation in their cognitive

functioning (e.g., Bradley et al., 1989; Brooks-Gunn, Klebanov & Duncan, 1996). Furthermore, Bradley et al. (1993) and Yeates et al. (1997) have identified a relationship between aspects of the home environment and cognitive functioning that may vary as a function of the child's CNS integrity in both low birthweight children and children who have suffered traumatic brain injury. Specifically, home environmental variables (e.g., play/learning materials, parental involvement, language stimulation) played a mediating role between maternal IQ and child IQ in low birthweight children (Bradley et al., 1993). Bradley suggested that this mediation does not represent the full causal relationship regarding intellectual functioning and other contributing factors should be investigated (e.g., family composition, crowding).

Only two studies (i.e., Coscia et al., 2001; Kullgren et al., 2004) have examined home environment variables as potential risk or protective factors related to the intellectual functioning of children with HIV. Coscia et al. (2001) found that the association between home environment (i.e., cognitive stimulation in the home; parental involvement; organization of the environment) and child intellectual functioning (measured by the MSCA, WPPSI-R, or WISC-III) varied as a function of the child's HIV illness severity. Specifically, for children in more advanced stages of the disease, the effect of the home environment on child intellectual functioning was magnified. Additionally, Kullgren et al. (2004) identified a significant cross-sectional relationship between SES and cognitive functioning that was mediated by the adult-to-child ratio at home. Interestingly, illness did not play a significant role in the prediction of cognitive functioning within the Kullgren sample. These studies illuminate the need for further identification of home environment variables that contribute to cognitive functioning associated with pediatric HIV. Through the identification of these variables, risk factors, and potential points of intervention for these children and their families will become more evident. Given the inconsistent findings in

several areas of functioning and the significant finding relating intellectual functioning and home environment variables (i.e., Coscia et al., 2001; Kullgren et al., 2004), it is foreseeable that similar relationships may exist between home variables and language functioning and attention/hyperactivity. As such, the present study will continue to explore the relationship between familial variables and child functioning (i.e., intellectual, language, and behavioral). Specifically, I will longitudinally examine the influence of the loss of the child's caregiver to death and the adult-to-child ratio in the home on cognitive functioning.

Children under the age of 13 years are usually (86%) infected with HIV perinatally (CDC, 2001). Thus, in addition to their own illness, these children experience the effects of maternal illness and perhaps maternal death. The emotional repercussions of losing one's mother and the practical disruptions that often result may compromise functioning. For example, as mothers become increasingly ill or die, the child may be placed with an alternative caregiver. In some situations, residential placement may involve the HIV-infected child entering a pre-existing family that already contains some number of children, perhaps negatively affecting the adult-to-child ratio in the home. Unfortunately, the empirical literature examining these family factors and intellectual, language, and attention is sparse and, in some cases, nonexistent. Thus, the family variables included in the study were chosen based on theoretical support of their importance.

Theoretical models. There are currently no HIV-specific models positing the ways in which illness and family factors combine to influence cognitive outcomes in HIV-infected children. The studies examining cognitive functioning in these children have combined illness and environmental factors as predictors of risk without providing a specific theoretical rationale (i.e., Bose et al., 1994; Henry et al., 1996; Coscia et al., 2001). Perhaps an HIV-specific model

will be born out of the individual scientific contributions of many. One avenue for incorporating relevant theory into the pediatric HIV literature is to rely on the general chronic illness literature for a model. There are three models that aim to explain adjustment in children with a chronic illness: the life-crisis model (Moos & Tsu, 1984), the disability-stress-coping model (Wallander & Varni, 1998), and the transactional stress and coping model (Thompson, Gustafson, George, & Spock, 1994). Although each model incorporates illness and elements of the child's environment in an attempt to better understand ill children's psychological adjustment, these models have not typically been used when predicting cognitive functioning outcomes. However, each model does contribute to the present study's conceptualization with respect to selection of predictor variables. Specifically, all three models suggest that aspects of the child's illness, including severity, course, and treatment, can influence outcomes. Furthermore, the models converge in that aspects of the child's environment, including family variables, can contribute to adaptation, either as a risk factor or a protective factor.

Outside of the chronic illness literature, Bronfenbrenner's Ecological Systems Theory (Bronfenbrenner, 1979), recently renamed the bioecological systems theory, does include cognitive functioning when considering child outcomes. According to Bronfenbrenner, a child develops within the context of the system of relationships that form his/her environment. Though a child's development is posited to begin with biological influences, her/his biological development (microsystem) takes place within the context of the family and home (mesosystem), and is fueled and guided by his/her society, culture, and community (exosystem). The current study targets two systems specified by Bronfenbrenner and supported by the other previously mentioned models: biology/illness and the family variables. The human body is part of Bronfenbrenner's microsystem. It enables an individual's mobility, perceptions, and interactions

with the environment, in addition to being the life support system. A person's general health/illness and bodily function, in the face of environmental factors, influences development. Brain insult, due to trauma or disease, is a specific aspect of health that can greatly influence the developmental process. The child's illness severity (i.e., CDC Classification system) is the biological factor considered in the present study.

The family is the most influential part of the mesosystem. The influences of the family extend to all aspects of the child's development, to include language and health. Two family variables will be considered in this study (i.e., caregiver death, adult-to-child ratio), each of which is particularly relevant for the lives of children living with HIV. The direct effects of the illness and family variables are examined, as are the interactive effects.

With regard to cognitive development, Bronfenbrenner's ecological systems can be mapped onto Piaget's stages of cognitive development. For infants in the sensorimotor stage, the microsystem and most immediate aspects of the mesosystem (e.g., family) are most pertinent to development. During the early childhood preoperational stage, when language develops, more of the mesosystem is incorporated. Then, the older child enters the concrete operational stage, and school and community are more directly influential. Finally, after age 12, the child enters the formal operational stage of cognitive development and the various aspects of the exosystem and macrosystem become more relevant to him/her. The typical child who participated in the current study was in the preoperational stage of cognitive development when first enrolled. Therefore, it stands to reason that aspects of the microsystem (e.g., illness, health) and mesosystem (e.g., family, home) are most important to incorporate as variables of interest.

Loss of caregiver. Perhaps the greatest devastation of AIDS for many children is the loss of their mothers (Mellins & Ehrhardt, 1994; Wiener, Havens, & Ng, 2003) and other caregivers.

This loss is often emotionally and logistically devastating. Furthermore, for a child who is aware that they share the illness with their deceased mother, death may bring fear and an intense brush with their own mortality. Rotheram-Borus and colleagues (1997) noted that children, in general, who have recently lost a family member may display symptoms of emotional disturbance and have poor academic performance. One study has demonstrated specifically that children whose mothers die due to HIV typically show an increase in their emotional, behavioral, and academic difficulties (Bachanas, Kullgren, Morris, & Jones, 1998). Thus, the current study considers the influence of caregiver loss to death individually, as well as the way this factor may interact with illness severity to influence child cognitive functioning.

Adult-to-child ratio. Regardless of with whom a child lives, the ratio of adults to children in the home is an important variable to consider. In fact, Dunn (1993) found a direct relationship between the adult-to-child ratio and IQ in a day care sample. Among African-American families, of which the present study is largely comprised, child rearing is often a communal responsibility shared by several adults who may or may not be related to the child in the traditional sense (for a review, see Forehand & Kotchick, 1996). Limited resources and maternal illness may negatively influence a child's support when the mother is the primary caregiver. Therefore, more adults in a household may buffer the negative effects of maternal HIV on child functioning by providing increased resources for the child (i.e., consistent parenting, basic care taking, and parental involvement). These additional caregivers are also likely to become primary caregivers when the mother's health fails.

Pequegnat and Bray (1997) proposed that the impact of maternal HIV on child adjustment may be assuaged by the presence and involvement of other adults who can assist with child care taking responsibilities. Three empirical studies to date have examined the role of

family structure as a protective factor for children in families coping with HIV. In the first study, a higher ratio of adults-to-children per household was associated with higher maternal ratings of child cognitive competence by HIV-infected mothers (Dorsey et al., 1999). However, in the second study, Biggar et al. (2000) failed to find a significant relationship between the ratio of adults-to-children in the home and a more objective measure of cognitive competence (i.e., grades in school) among children of HIV-infected mothers. Lastly, Kullgren et al. (2004) cross-sectionally examined the relationship between adult-to-child ratio and objectively assessed cognitive functioning in children with HIV infection. Specifically, they found that the adult-to-child ratio mediated the relationship between SES and cognitive functioning, as measured by Full Scale and Verbal Scale IQ of the WISC-III, WPSI-R, or McCarthy. Kullgren and colleagues also identified the adult-to-child ratio as a significant predictor of adaptive behavior (i.e., Vineland Adaptive Behavior Composite, Communication Skills, Socialization Skills). However, possible interaction effects among adult-to-child ratio, child's HIV illness severity, and cognitive functioning have not been investigated, nor have they been examined across time. The present study seeks to add to knowledge in the pediatric HIV field by exploring these longitudinal relationships.

Chemical Influences

Prenatal drug exposure. The most common modes of HIV transmission among women are intravenous (IV) drug use and unprotected sex with IV drug using partners (CDC, 2001), which in turn may expose HIV-infected infants to drugs in utero. Although the present study will not include in utero drug exposure as a variable of interest, it is important to acknowledge that it may contribute to the functioning of the children in the study sample. Research findings of the additive effects of HIV and prenatal drug exposure have been contradictory with three

typical outcomes. Some studies (e.g., Levenson et al., 1992) are indicative of no differences on global measures of cognitive functioning between drug exposed and non-drug exposed HIV-infected children. Other studies (e.g., Henry et al., 1996) found that prenatal drug exposure accounted for a significant amount of the variance in cognitive functioning in children, regardless of serostatus. The third set of studies provides evidence that HIV infection compromised cognitive functioning beyond the influence of in utero drug exposure. For example, Mellins et al. (1994) reported that prenatal drug exposure combined with HIV-infection resulted in poorer global cognitive functioning than was seen in seroreverters or infants with drug exposure only. The scope of the current study will not extend to the examination of the additive effects of HIV and in utero drug exposure. However, where possible, descriptive information about prenatal drug exposure will be provided.

Medication treatment of HIV. Since the use of highly active antiretroviral therapy (HAART) became widespread in the US in 1996, many patients are being treated with this combination therapy. HAART is generally a combination of three medications, including a protease inhibitor and/or nonnucleoside reverse transcriptase inhibitor. As HIV/AIDS treatment has progressed, it appears that monotherapy is superior to no treatment (Lewis, et al., 1996), dual-therapy is superior to monotherapy (McKinney, et al., 1998), and combination therapy that includes a protease inhibitor is superior to dual-therapy (Yogev, et al., 2002) in terms of virology and immunology. Furthermore, significant improvements have been seen in cognitive, adaptive, and behavioral functioning following the initiation of protease inhibitor combination antiretroviral therapy in some samples (e.g., Tepper et al., 1998). The current study will consider the effects of current medication therapy on outcome variables, but the impact of medication treatment for these children will not be a primary focus.

Summary and Hypotheses

African-American children are disproportionately represented among pediatric HIV cases in the United States. Additionally, they are, by and large, an under-served and understudied group. Thus, the sample for the current study is constituted primarily by HIV-infected African-American children. While much research indicates that HIV negatively affects intellectual, language, and attentional/ hyperactivity functioning, some researchers have not found such effects, particularly when examining global cognitive functioning. Furthermore, as HIV illness severity increases, functioning in a number of areas typically declines. A number of factors (e.g., familial factors), other than severity of HIV, as suggested by Bronfenbrenner's Ecological Systems theory, may contribute to inconsistent findings in the literature on cognitive functioning. The first purpose of this study is to provide information about the extent to which cognitive functioning changed over time and/or differed across gender. Based on the literature, girls were expected to have higher verbal intellectual functioning than boys. Conversely, boys were expected to perform better than girls on performance intelligence areas (specifically, visual-spatial and mathematical abilities) (Maccoby & Jacklin, 1974). Expectations about children's performance at Time One versus Time Two for intellectual functioning are unclear because of the limited guiding literature. One possibility is that if children become more ill over time, their IQ scores may decline. An alternative possibility is that with longer use of more advanced anti-HIV medications, children's IQ scores may improve. Likewise, the direction of a main effect for gender on language functioning is difficult to predict because of a lack of guiding literature. However, a decline was expected in both expressive and receptive language functioning over time based on Wolters et al. (1997) findings. Because the measure of attention/hyperactivity functioning changed during the course of this study, analyses of changes over time would not be

appropriate. The author does expect to find higher scores for boys than girls, indicating more severe difficulties in this area of functioning (Conners, 1990 and 1997).

Familial and home environment variables are demonstrated contributors to child functioning in other samples, and are beginning to be explored in the pediatric HIV literature. The HIV-infected family presents a unique situation in that the illness often afflicts both child and caregiver. Literature regarding the influence of child HIV-illness severity, familial variables, and functioning is in its infancy (Coscia et al., 2001; Dorsey et al., 1999; Kullgren et al., 2004). A previous study (Kullgren et al., 2004) utilized many of the same children as the current author. This previous study was cross-sectional in design and explored the additive influence of background, illness, and environmental factors as predictors of cognitive, adaptive, and behavioral functioning. The second purpose of the current study is to longitudinally examine the individual and interactive influence of illness severity and familial variables on cognitive functioning in children with HIV infection. As Time One functioning will be controlled, these analyses represent a conservative exploration of longitudinal relationships. More specifically, while partialling out the expected large effects of Time One outcome variables, the author anticipates finding a significant association between favorable familial variables at Time One (e.g., more adults per child in a household, fewer caregiver deaths, greater length of time since caregiver death) and better cognitive outcomes at Time Two (i.e., Coscia et al., 2001; Kullgren et al., 2004: Rotheram-Borus et al., 1997). Because most (Loveland et al., 2000; Nozyce, et al., 1994; Pollack et al., 1996), though not all (e.g., Kullgren et al. 2004) research demonstrated a relationship between illness severity and cognitive outcomes, I expect that as illness severity increases, cognitive performance will decline, when the effects of Time

One outcome variables are controlled. The possible interactive effects of Time One familial variables and Time Two illness severity on cognitive outcomes at Time Two is exploratory.

CHAPTER TWO: METHOD

Participants

Participant background information is presented in Table 1. Forty-two perinatally HIV-infected children (12 boys, 30 girls) and their caregivers participated. Participants were children who received care at the Pediatric Infectious Disease Program of Grady Healthcare System, an urban, multidisciplinary setting, and their primary caregivers. Typical caregivers were not employed. Specifically, participants included caregivers of and children who 1) were between 3 and 12 years of age at the time of the first assessment; 2) were perinatally infected with HIV; 3) spoke English as their primary language; and 4) had been administered the measures used in this study after 1998. Although all child participants were perinatally infected with HIV, many were diagnosed after infancy. Thirty-nine children were African-American, two were Caucasian-American, and one was of another race. Given the small sample size and that only three children were not African-American, all participant data are examined together in this sample. Prenatal drug exposure information was available for 83% of this sample. Of those children, over half (57.1%) had documented prenatal drug exposure (e.g., alcohol, marijuana, cocaine) based on either caregiver report or a positive laboratory drug screen at birth.

Illness severity. Illness severity information was obtained from medical charts. Each child's HIV illness was classified according to the Centers for Disease Control and Prevention Classification Criteria (CDC, 1994). The HIV Stage of Illness Classification Criteria categorizes individuals into one of twelve categories, based on four clinical categories of symptomatology

Table 1

Participant Background Characteristics (n=42)

	Percent	M	SD	Range
Age at Time One (months)		72.4	24.1	39-142
Age at Time Two (months)		96.5	25.6	66-172
Female	71.4			
African-American	92.9			

and three ranges of CD4+ T-lymphocyte counts (a decrease in CD4+ T-lymphocytes is associated with increased severity of illness). At Time One, approximately 71% of children had mild to moderate clinical symptoms of HIV and 83% had moderate to severe immune suppression. According to the 1993 CDC AIDS case definition, an HIV-infected person is diagnosed with AIDS when he/she has a CD4+ count of less than 200 cells per microliter or when CD4+ cells account for fewer than 14 percent of all lymphocytes. For the purposes of this study, viral load was used as the marker of HIV illness severity. At the beginning of this study, participants' mean CD4+ count was 971 (SD = 582, range = 286-2,633) and mean viral load was 50,978 (SD = 147,287, range = 400-750,000). At the second assessment point, participants' mean CD4+ count was 897 (SD = 419, range = 366-2024) and mean viral load was 7,693 (SD = 10,774, range = 400-41,930).

Medication. Information about the medications prescribed for treatment of HIV was gathered from medical charts at each assessment point. Type of medication was categorized as highly active antiretroviral therapy (HAART), which generally included a protease inhibitor (Time One n=24, 57.1%; Time Two n=34, 81%), or not HAART, which included no medication (Time One n=1, 2.4%; Time Two n=0, 0%), monotherapy (Time One n=2, 4.8%; Time Two n=1, 2.4%), and dual therapy regimens (Time One n=15, 35.7%; Time Two n=7, 16.7%). A variable was created which indicated the percentage of the child's life during which s/he has been on the HAART regimen (i.e., time on regimen/lifetime [in months]).

Family variables. Familial factors included information regarding loss of caregivers to death and the adult-to-child ratio in the home. This information was gathered either through medical charts or clinical interviews conducted with the caregiver as part of each assessment.

The specific loss of caregiver variables of interest were 1) how many guardians had the child lost to death, and 2) how long before the assessment did the most recent caregiver die. This information was gathered at each assessment point. When the year of death was known (N of 3), but not the month, the middle of the given year was assumed. At Time One, 31% of the participants had lost one caregiver to death on average 31 months before the assessment.

Regarding the adult-to-child ratio, any person 18 years of age or older was considered an adult and contributed one unit to the numerator. Each person under the age of 18 contributed one unit to the denominator. At Time One, 59.5% of participants lived in homes as the only child or with only one other child (range of total children in the home = 1-7). Ninety-three percent of children resided with one or two adults (range of adults in the home = 1-3). Similarly at Time Two, 52.4% of participant homes included one or two children (range 1-9 children), and 92.9% had one or two adults (range 1-3 adults).

Procedure

A retrospective archival design was used for this study. Children received psychoeducational evaluations as part of their regular multidisciplinary care. The results of these evaluations, along with other information pertaining to the children's medical care and family, were gathered from the children's medical charts. Assessments were conducted between January 1998 and January 2004.

As part of their standard care, each child was individually administered a three- to four-hour comprehensive assessment battery approximately every 12 to 18 months. The child's caregiver was asked to complete a behavioral functioning measure (Conners' Parent Rating Scale – Short original or revised version) on the child and a semi-structured interview, with the same clinician, either at the time of the assessment or by telephone soon thereafter. Clinicians read the behavioral functioning measure to those parents who needed assistance. Graduate or post-graduate psychology clinicians, who were supervised by a licensed clinical psychologist, conducted assessments and interviews. The information from two consecutive assessments for each participant was utilized in this study, with no more than 36 months between assessment points (mean number of months between assessments = 24).

In order to preserve confidentiality, all participants were assigned an identification number and coded accordingly. Per the Institutional Research Board of Georgia State University and Emory University, participant's previous consent to treatment as patients at the IDP was adequate for this study. Therefore, no additional informed consent was obtained and information was entered into the database and reported such that confidentiality was ensured. Participants were treated in accordance with the "Ethical Principles of Psychologists and Code of Conduct" (American Psychological Association, 1992).

Outcome Measures

Intellectual functioning. Intellectual functioning was measured by either the Wechsler Intelligence Scale for Children (Third Edition) (WISC-III; Time One n=14, Time Two n=31) (Wechsler, 1991) or the Wechsler Pre-School and Primary Scale of Intelligence-Revised (WPPSI-R; Time One n=28, Time Two n=11) (Wechsler, 1989), depending on the child's age at the time of the assessment. The WISC-III is a standardized measure of intellectual functioning for children ages 6 years to 16 years, 11 months, whereas the WPPSI-R is used with children ages 3 years to 7 years, 3 months. For the purposes of this study, global, verbal, and performance intelligence were considered (Full Scale IQ, Verbal IQ, and Performance IQ, respectively). The WISC-III and WPPSI-R have both been shown to have adequate reliability and validity (Wechsler, 1989 and 1991). The WISC-III and WPPSI-R were normed on a sample that was representative of the United States population of children (Wechsler, 1989 and 1991).

As no single measure spans the age-range of the participants, combining data from different measures of intellectual functioning across participants was sometimes necessary. Following the example of previous research with HIV-infected children, the scores from these different measures were combined across subjects into intellectual index scores for global, verbal, and performance abilities (Brouwers, Tudor-Williams, et al., 1995; Brouwers et al., 1990; Diamond et al., 1990; Wolters et al., 1997). The WPPSI-R and WISC-III correlate highly on FSIQ (r=.85), VIQ (r=.85), and PIQ (r=.73), thereby indicating that they measure largely very similar constructs (Wechsler, 1991).

Language functioning. Language functioning was measured with either the Expressive One-Word Picture Vocabulary Test – Revised (Gardner, 1990) or Expressive One-Word Picture Vocabulary Test – Third Edition (Brownell, 2000a), and the Receptive One-Word Picture

Vocabulary Test (Gardner, 1985) or Receptive One-Word Picture Vocabulary Test – Second Edition (Brownell, 2000b). These measures have been standardized on children age 2 years to 18 years, 11 months. On the EOWPVT-R and EOWPVT-3, children are shown illustrations that depict an object, action, or concept. They are asked to name each illustration. On the ROWPVT and ROWPVT-2, children are shown four illustrations simultaneously and asked to identify the one that depicts the stimulus word provided by the examiner. These expressive and receptive measures have been found to have adequate reliability and validity (Brownell, 2000a; Brownell, 2000b; Gardner, 1985; Gardner, 1990), and have been used in other studies of HIV-infected children. The measures were normed on a nationally representative sample of individuals residing in the United States (Brownell, 2000a; Brownell, 2000b; Gardner, 1985; Gardner, 1990).

Attention/hyperactivity difficulties. The Conners' Parent Rating Scales (Short) (Conners, 1990) or the Conners' Parent Rating Scales – Revised (Short) (Conners, 1997) was administered to assess attentional and hyperactivity problems. The original measure includes 48 Likert-scale items that load on five factors – Conduct Disorder, Learning Problem, Psychosomatic, Impulsive-Hyperactivity, and Anxiety. Originally thought of as a measure of hyperactivity, the Hyperactivity Index is now understood to consist of select items from the five factors that combine to create a general index of child psychopathology. The revised measure consists of 27 Likert-scale items that load on four factors – Oppositional, Cognitive Problems/Inattention, Hyperactivity, and ADHD Index. On both the original and revised measures, gender and age specific norms are available for children ages 3 to 17 years. Caregivers rate symptoms on a four-point scale ranging from "Not true at all (Never, Seldom)" to "Very much true (Very Often, Very Frequent)". The raw scores on each factor are transformed into T-scores based on norms

reported by Goyette, Conners, & Ulrich (1978) and Conners (1997) for the revised version. This original measure has been used to assess behavioral functioning in other studies of children infected with HIV (Bose et al., 1994; Moss et al., 1998), and has been reported to have adequate reliability and validity (Sattler, 1992). However, it is noteworthy that the original Conners' was normed on a sample of primarily Caucasian-Americans (98%) (Goyette et al., 1978), and may not provide an appropriate comparison group for ethnic minority children. Alternatively, the revised Conners' was normed on a representative sample of the North American population.

As the children in this study are provided care throughout their lifetime, the revised version was incorporated into the standard of care during the course of this study. At Time One, thirty of the study participants received the original Conners', and nine received the revised Conners'. Conversely, at Time Two, 37 participants had scores for the revised Conners', and only three had scores for the original Conners'. The tests' developers caution that despite many similarities between the two versions, the original and revised versions should be treated as separate instruments and not compared directly. In order to at least partially address this issue, the author chose the scale from each measure that most closely represented the construct in question. For the original Conners' this was the Hyperactivity Index, and the ADHD Index was chosen for the revised Conners'. These scales each include attention and hyperactivity items, although the Hyperactivity Index of the original Conners' is inclusive of other general child psychopathology as well. A unique variable of attentional/hyperactivity difficulties was created for this study by collapsing data from the two scales and utilizing t-scores to standardize the measurement scale.

CHAPTER THREE: RESULTS

Prior to analyses, all outcome variables were examined for accuracy of data entry, missing values, and outliers (defined as values more than three standard deviations from the sample mean). The means, standard deviations, and ranges of all outcome variables are presented in Table 2 and 3. There were no outliers or missing data at either assessment point for Full Scale IQ, Verbal IQ, or Performance IQ. For the EOWPVT and ROWPVT at Time One, no outliers were identified and no data were missing. For the language measures at Time Two, no outliers were identified, but three participants (7.1%) did not complete these measures. The Time Two sample mean was substituted for the missing values on both measures. There were no outliers at either assessment point for the measure of attention/hyperactivity functioning. However, the three missing data points at Time One and two missing data points at Time Two were replaced with the sample mean at the respective assessment points.

Descriptive Findings

Mean global (FSIQ), verbal (VIQ), and performance (PIQ) functioning at Time One and Time Two fell more than one standard deviation below the mean of the normative sample (see Table 2). Scores ranged from mentally deficient to superior intellectual functioning. More specifically, at Time One for FSIQ and PIQ 62% (n=26) of the sample fell more than one standard deviation below the normative mean, 36% (n=15) were within the normative range, and 2% (n=1) were more than one standard deviation above the normative sample mean. For Time One VIQ, 60% (n=25) of the sample fell more than one standard deviation below the normative

Table 2

Intellectual and Language Functioning Standard Scores at Time One and Time Two (n=42)

	M	SD	Range
Time One			
Full Scale IQ	79.48[a]	14.98	52-124
Verbal IQ	81.17[a]	14.34	53-119
Performance IQ	81.36[a]	14.31	52-122
Expressive Language	82.69[a]	15.80	55-127
Receptive Language	88.07	14.96	55-117
Time Two			
Full Scale IQ	80.71[a]	14.80	57-112
Verbal IQ	80.31[a]	14.35	55-111
Performance IQ	84.83[a]	16.22	56-130
Expressive Language	86.86	18.25	55-129
Receptive Language	89.29	17.60	55-135

Note. [a] More than one SD below normative sample mean (M = 100, SD = 15).

mean, 38% (n=16) were within the normative range, and 2% (n=1) were more than one standard deviation above the normative mean.

The language functioning descriptive statistics are presented in Table 2. Mean expressive language functioning fell more than one standard deviation below the mean of the normative sample at Time One, but within one standard deviation of the normative mean at Time Two. Expressive language functioning scores ranged from mentally deficient to superior. Mean receptive language functioning at Time One and Time Two were not considerably different from the normative sample, and ranged from mentally deficient to superior. More specifically, for Time One EOWPVT, 55% (n=23) of the sample fell more than one standard deviation below the normative mean, 43% (n=18) were within the normative range, and 2% (n=1) were more than one standard deviation above the normative mean. For Time One ROWPVT, 36% (n=15) of the sample fell more than one standard deviation below the normative mean, 62% (n=26) were within the normative range, and 2% (n=1) were more than one standard deviation above the normative mean.

Regarding attentional/hyperactivity functioning, at Time One and Time Two, the sample mean was not considerably different from the normative sample of either the Hyperactivity Index of the original Conners' or the ADHD Index of the revised Conners' (see Table 3). Scores ranged from mildly atypical-low (low scores are good: not a concern) to markedly atypical-high (indicates significant problems). For Time One attention/hyperactivity functioning, none of the sample fell more than one standard deviation below the normative mean, 67% (n=28) were within the normative range, and 33% (n=14) were more than one standard deviation above the normative mean. So, 33% of the sample was experiencing some attentional/hyperactivity problems.

Table 3

Attention/Hyperactivity Functioning Standard Scores at Time One and Time Two (n=42)

	M	SD	Range
Time One			
Attention/hyperactivity	57.23	14.18	40-99
Time Two			
Attention/hyperactivity	57.26	10.56	39-86

Note. Normative sample (M = 50, SD = 10).

Preliminary Analyses

Correlations among variables were calculated based on demographic, Time One family variables, Time Two illness severity and medication variables, and Time Two outcome variables. These correlations are presented in Table 4. None of the demographic (i.e., age, gender) or Time Two medication variables (i.e., medication category, percentage of lifetime on HAART) were significantly correlated with any of the Time Two outcome variables. The relationship between the adult-to-child ratio and ROWPVT was the only significant correlation between a predictor variable (i.e., illness severity and familial variables) and a Time Two outcome variable. Specifically, as the number of adults per child in a home increases at Time One, there is a corresponding increase in ROWPVT performance at Time Two.

Table 4

Correlations Among Demographic, Time Two Medical, Time One Predictor, and Time Two Outcome Variables

Measures	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 Sex	1.00	.140	.038	-.297	-.162	-.087	.195	.129	-.099	-.079	-.099	-.233	-.159	.046
2 Age		1.00	-.116	-.202	-.151	-.183	.312*	.411**	-.184	-.214	-.134	-.023	-.099	-.016
3 Medication category			1.00	-.516**	-.036	.209	-.194	-.139	.287	.284	.224	.159	.145	.063
4 % of life on HAART				1.00	-.272	-.024	-.149	-.119	-.120	-.012	-.202	-.087	.022	.068
5 Viral load					1.00	.015	.064	.035	-.023	-.071	.018	.121	-.007	.229
6 Adult/child ratio						1.00	-.175	-.175	.282	.267	.251	.258	.484**	-.101
7 # caregivers lost							1.00	.795**	-.163	-.113	-.154	-.038	-.239	-.086
8 # months since last caregiver lost								1.00	-.090	-.073	-.103	-.027	-.134	-.018
9 Full Scale IQ									1.00	.906**	.915**	.711**	.676**	-.067
10 Verbal IQ										1.00	.669**	.701**	.631**	.065
11 Performance IQ											1.00	.575**	.591**	-.168
12 Expressive language												1.00	.563**	-.112
13 Receptive language													1.00	-.019
14 Attention/hyperactivity functioning														1.00

Note. **p<.01, *p<.05

Primary Analyses

A previous study with a sample drawn from this same population (Kullgren et al., 2004), examined cognitive, adaptive, and behavioral functioning cross-sectionally. The present study expands on that work, first by describing changes in child functioning over time and across genders. Specifically, 2 (assessment period) X 2 (gender) mixed between-within subjects ANOVAs were conducted with assessment serving as the within subjects variable and gender as the between subjects variable. FSIQ, VIQ, PIQ, EOWPVT, and ROWPVT served as the dependent variables. No demographic (i.e., age) or Time Two medical variables (i.e., medication category, percentage of lifetime on HAART, illness severity) were significantly correlated with the Time Two outcome variables; therefore, analyses of covariance were not necessary. The means and standard deviations are presented in Tables 5, 6, 7, 8, and 9.

There was not a significant main effect for gender (FSIQ $F(1,40) = .35$, $p > .05$; VIQ $F(1,40) = .21$, $p > .05$; PIQ $F(1,40) = .42$, $p > .05$) or time (FSIQ $F(1,40) = .73$, $p > .05$; VIQ $F(1,40) = .26$, $p > .05$; PIQ $F(1,40) = 2.94$, $p > .05$), nor a significant interaction effect between gender and time for any of the intellectual functioning outcomes (FSIQ $F(1,40) = .04$, $p > .05$; VIQ $F(1,40) = .05$, $p > .05$; VIQ $F(1,40) = .03$, $p > .05$). With regard to expressive language, there was a significant main effect for time with a moderate effect size (EOWPVT $F(1,40) = 5.03$, $p < .05$, effect size =). Specifically, the expressive language skills of both males and females improved over time. There was no significant main effect for gender ($F(1,40) = 1.72$, $p > .05$), nor a significant interaction effect ($F(1,40) = 1.03$, $p > .05$), for expressive language. However, there was a clinically relevant gender difference on expressive language, with girls, but not boys, performing more than one standard deviation below the normative sample at both assessment points. There were no significant main effects for gender ($F(1,40) = .00$, $p > .05$) or

time (F (1,40) = 1.96, p > .05) on receptive language, but there was a significant interaction effect with a moderate effect size (F (1,40) = 4.85, p < .05, effect size =). Specifically, over time males' receptive language skills improved, and females' receptive language skills declined. The male receptive language improvement over time is statistically significant (t(11)=-2.873, p<.05) with a large effect size (eta squared = .43); whereas the decline in female receptive language skills was not statistically significant (t(29)=.693, p>.05). Again, because of the difference in the measures used to assess attention/hyperactivity between Time One and Time Two, only gender differences were examined for this outcome variable. An independent samples t-test found no significant difference between males (Time One M=61.5, SD=13.43; Time Two M=56.5, SD=8.99) and females (Time One M=55.53, SD=14.33; Time Two M=57.57, SD=11.26) on attention/hyperactivity at Time One [t(40)=1.240, p>.05] or Time Two [t(40)=-.292, p>.05].

To address the second study question, do Time One family variables and Time Two illness severity either independently or interactively effect functioning at Time Two, six hierarchical regression analyses were conducted. The regressions represent a conservative exploration of interactive and longitudinal relationships and are presented in tables 10 through 15. In these analyses, the effects of the Time One outcome variables were controlled for before examining associations between familial variables, illness severity, and cognitive functioning. In addition, the interactions between illness severity and familial variables on outcomes were examined. Prior to conducting the regression analyses, correlations indicated no statistically significant relationships between the demographic or Time Two medication variables and the outcome variables at Time Two. Therefore, it was not necessary to control for the effects of demographic or medication variables in these regression analyses. As such, variables were

Table 5

Means and Standard Deviations for Gender and Time Variables on Full Scale IQ

Testing Time	Males	Females
Time One		
M	81.33	78.73
SD	20.84	12.26
Time Two		
M	83.00	79.80
SD	17.65	13.72

Table 6

Means and Standard Deviations for Gender and Time Variables on Verbal IQ

Testing Time	Males	Females
Time One		
M	82.50	80.63
SD	18.87	12.43
Time Two		
M	82.08	79.60
SD	16.60	13.59

Table 7

Means and Standard Deviations for Gender and Time Variables on Performance IQ

Testing Time	Males	Females
Time One		
M	83.33	80.57
SD	19.43	12.00
Time Two		
M	87.33	83.83
SD	18.22	15.57

Table 8

Means and Standard Deviations for Gender and Time Variables on Expressive Language

Testing Time	Males	Females
Time One		
M	86.00	81.37
SD	19.45	14.26
Time Two		
M	93.50	84.20
SD	22.58	15.88

Table 9

Means and Standard Deviations for Gender and Time Variables on Receptive Language

Testing Time	Males	Females
Time One		
M	84.08	89.67
SD	17.80	13.67
Time Two		
M	93.67	87.53
SD	20.42	16.38

entered in the following blocks: (1) Time One outcome variable; (2) Time Two illness severity (i.e., viral load) and Time One familial variables; and (3) the interactions between Time Two illness severity and Time One familial variables. In order to determine the relative standing of a measurement in the data set, the illness severity and familial variables were each centered and the centered terms were used independently and in the interaction terms. The three children who lost caregivers to death between the two assessments were not included in the regression analyses.

As reported in Table 10, the Time One FSIQ accounted for 64.5% ($p<.01$) of the variance in Time Two FSIQ. Taking Time One FSIQ into account, the combined illness and familial variables accounted for less than 1% of additional variance. When both the Time One FSIQ and the combined illness and familial variables were considered, the interactions between illness severity and the familial variables accounted for an additional 1.4% of the variance. The total

model was significant and accounted for 57% (adjusted R^2) of the variance in FSIQ in the sample [$F(8,30)=7.288$, $p<.01$]. However, other than FSIQ at Time One, none of the illness, familial, or interaction variables independently contributed a significant amount to the explanation of variance in FSIQ at Time Two.

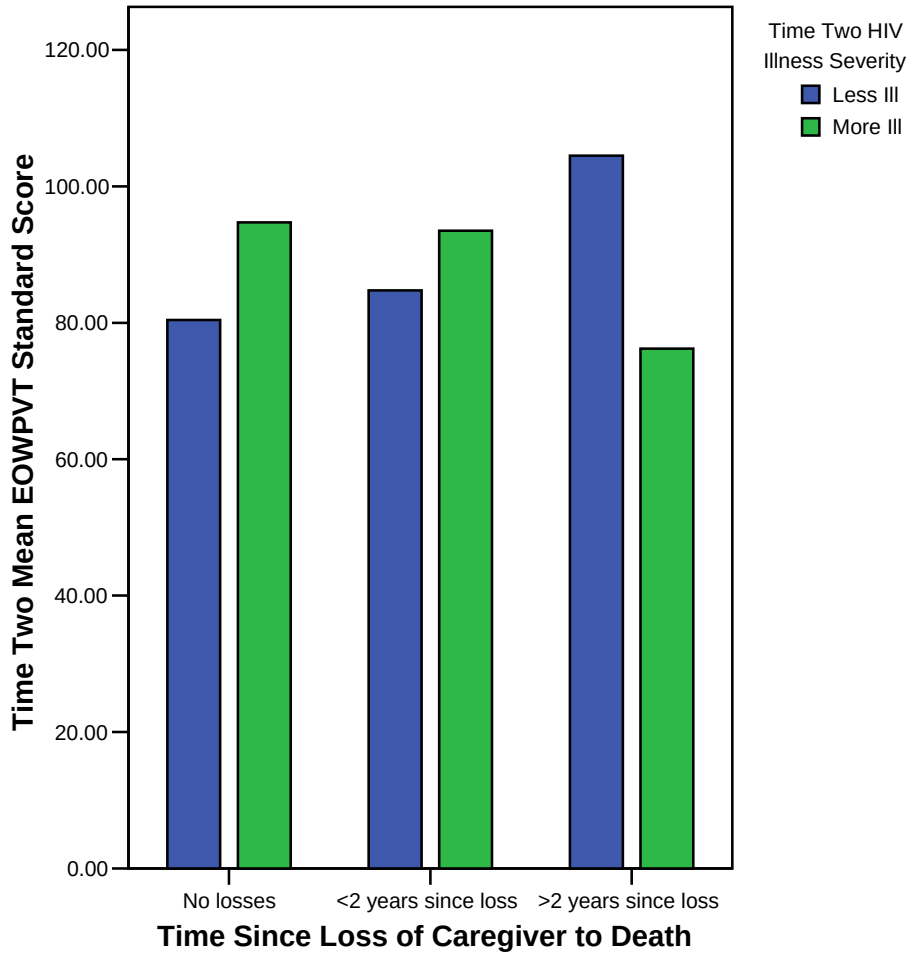
As reported in Table 11, the Time One VIQ significantly accounted for 68.8% ($p<.01$) of the variance in Time Two VIQ. Taking Time One VIQ into account, the combined illness and familial variables accounted for 1.2% of additional variance. When both the Time One VIQ and the combined illness and familial variables were controlled for, the interactions between illness severity and the familial variables accounted for less than 1% of the variance. The total model was significant and accounted for 63% (adjusted R^2) of the variance in VIQ in the sample [$F(8,30)=9.090$, $p<.01$]. However, other than VIQ at Time One, none of the illness, familial, or interaction variables independently contributed a statistically significant amount to the explanation of variance in VIQ at Time Two.

As reported in Table 12, the Time One PIQ significantly accounted for 50% ($p<.01$) of the variance in Time Two PIQ. Taking Time One PIQ into account, the combined illness and familial variables accounted for less than 1% of additional variance. When both the Time One PIQ and the combined illness and familial variables were controlled for, the interactions between illness severity and the familial variables accounted for 1.8% of the variance. The total model was significant and accounted for 39.2% (adjusted R^2) of the variance in PIQ in the sample [$F(8,30)=4.068$, $p<.01$]. Once again, other than PIQ at Time One (at each step of the regression), none of the illness, familial, or interaction variables independently contributed a significant amount to the explanation of variance in PIQ at Time Two.

As reported in Table 13, the Time One EOWPVT significantly accounted for 53.8% ($p<.01$) of the variance in Time Two EOWPVT. Taking Time One EOWPVT into account, the combined illness and familial variables accounted for 4.6% of additional variance. When both the Time One EOWPVT and the combined illness and familial variables were controlled for, the interactions between illness severity and the familial variables accounted for an additional 7.6% ($p=.10$) of the variance. The total model was significant and accounted for 57% (adjusted R^2) of the variance in EOWPVT in the sample [$F(8,30)=7.293$, $p<.01$]. At each step of the regression, Time One EOWPVT accounted for a significant portion of the variance independently. There was also a significant relationship between the interaction between number of months since caregiver death and illness severity and Time Two EOWPVT, when the effects of all of the variables in the regression equation were considered. To interpret this interaction, both independent variables were converted to categorical variables. With regard to the number of months since caregiver death, the categories were no loss of caregiver to death (n=29), less than 24 months since caregiver death (n=6), and more than 24 months since caregiver death (n=7). A categorical Time Two illness severity variable was created by performing a median split and grouping children into one of two categories based on Time Two viral load (less ill group viral load range 400-2,430; more ill group viral load range 3,440-41,930). Each group was comprised of 21 participants. Figure 1 graphically depicts the interaction. Specifically, among children who have not lost a caregiver to death, the more ill children perform better than the less ill children on an expressive language task. Among children who more recently lost a caregiver to death, there is not much difference between the less ill children's scores at Time Two and the more ill group. For the group of children with the greatest amount of time since caregiver death, the less ill children perform better than those who are more ill.

Figure 1

Mean Time Two Expressive Language by Time Since Death of Caregiver and Illness Severity



As reported in Table 14, the Time One ROWPVT significantly accounted for 25.4% ($p<.01$) of the variance in Time Two ROWPVT. Taking Time One ROWPVT into account, the combined illness and familial variables accounted for 16.2% ($p<.10$) of additional variance. When both the Time One ROWPVT and the combined illness and familial variables were controlled for, the interactions between illness severity and the familial variables accounted for an additional 9.7% of the variance. The total model was significant and accounted for 38.2%

(adjusted R^2) of the variance in ROWPVT in the sample [F(8,30)=3.938, p<.01)]. At each step of the regression, Time One ROWPVT accounted for a significant portion of the variance independently. There was also a significant relationship between the adult-to-child ratio and Time Two ROWPVT at the second and third steps of the regression (p=.04, p=.02, respectively). Specifically, as the number of adults per child in a home increases at Time One, there was an increase in the child's receptive language functioning at Time Two. Furthermore, there was a statistically significant (p=.04) relationship between the interaction between number of months since caregiver death and illness severity and Time Two ROWPVT, when the effects of all of the variables in the regression equation were considered. To interpret this interaction, the same categorical variables were used as in the expressive language model. Figure 2 graphically depicts the interaction. Specifically, among children who have not lost a caregiver to death, the more ill children perform better than the less ill children on a receptive language task. Among children who more recently lost a caregiver to death, there is not much difference between the less ill children's receptive language scores at Time Two and the more ill group. For the group of children with the greatest amount of time since caregiver death, the less ill children perform better than those who are more ill.

Because Time One and Time Two attention/hyperactivity were not significantly correlated, Time One attention/hyperactivity was not controlled in this hierarchical regression (see Table 15). The combined illness and familial variables accounted for 9.6% of the variance in Time Two attention/hyperactivity scores. When the combined illness and familial variables were controlled for, the interactions between illness severity and the familial variables accounted for an additional 8.2% of the variance. The total model was not statistically significant [F(8,30)=.962, p=.48)]. None of the illness, familial, or interaction variables independently

contributed a significant amount to the explanation of variance in attention/hyperactivity at Time Two.

Figure 2

Mean Time Two Receptive Language by Time Since Death of Caregiver and Illness Severity

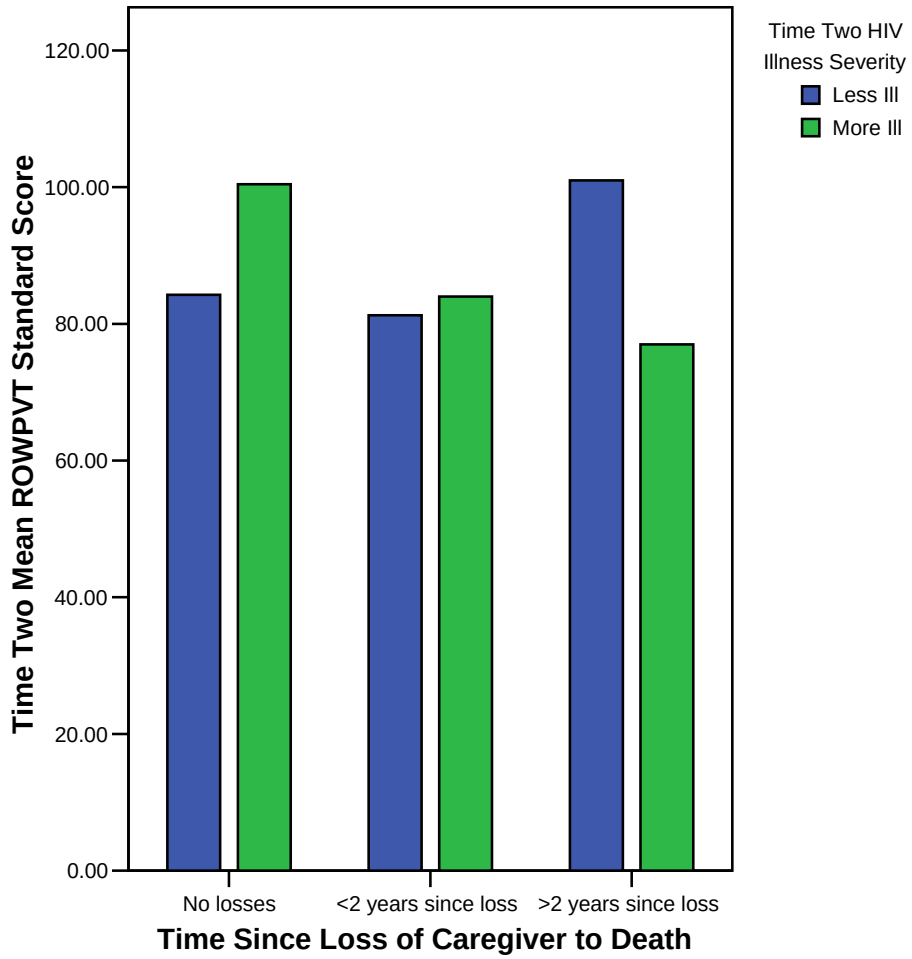


Table 10

Hierarchical Multiple Regression on Full Scale IQ at Time Two

Variables	Step 1 Full Scale IQ at Time One	Step 2 Illness Severity & Familial Variables	Step 3 Interactions
FSIQ Time 1	.803*	.803*	.778*
Viral load at Time 2		.008	.016
Adult-to-child ratio Time 1		-.006	.008
# Caregivers lost to death Time 1		-.019	-.009
# Months since caregiver loss Time 1		-.022	-.030
Interaction ratio x viral load			.056
Interaction # caregivers x viral load			-.083
Interaction # months x viral load			-.023
Adjusted R^2	.635	.593	.570
ΔR^2	.645*	.001	.014
F	67.200*	12.064*	7.288*

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. *$p<.0005$

Table 11

Hierarchical Multiple Regression on Verbal IQ at Time Two

Variables	Step 1 Verbal IQ at Time One	Step 2 Illness Severity & Familial Variables	Step 3 Interactions
VIQ Time 1	.829*	.856*	.851*
Viral load at Time 2		-.018	-.009
Adult-to-child ratio Time 1		-.036	-.036
# Caregivers lost to death Time 1		.115	.130
# Months since caregiver loss Time 1		-.168	-.182
Interaction ratio x viral load			.018
Interaction # caregivers x viral load			-.119
Interaction # months x viral load			.063
Adjusted R^2	.680	.654	.630
ΔR^2	.688*	.012	.008
F	81.582*	15.371*	9.090*

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. *$p<.0005$

Table 12

Hierarchical Multiple Regression on Performance IQ at Time Two

Variables	Step 1 Performance IQ at Time One	Step 2 Illness Severity & Familial Variables	Step 3 Interactions
PIQ Time 1	.707**	.699**	.679**
Viral load at Time 2		.036	.042
Adult-to-child ratio Time 1		.022	.037
# Caregivers lost to death Time 1		-.030	-.021
# Months since caregiver loss Time 1		.014	.006
Interaction ratio x viral load			.064
Interaction # caregivers x viral load			-.060
Interaction # months x viral load			-.063
Adjusted R^2	.487	.427	.392
ΔR^2	.500**	.002	.018
F	37.053**	6.668**	4.068*

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. **p<.0005, *p=.002

Table 13

Hierarchical Multiple Regression on Expressive Language at Time Two

Variables	Step 1 Expressive Language at Time One	Step 2 Illness Severity & Familial Variables	Step 3 Interactions
EOWPVT Time 1	.734**	.749**	.665**
Viral load at Time 2		.064	.059
Adult-to-child ratio Time 1		.070	.121
# Caregivers lost to death Time 1		-.021	-.033
# Months since caregiver loss Time 1		-.167	-.134
Interaction ratio x viral load			.131
Interaction # caregivers x viral load			.153
Interaction # months x viral load			-.352*
Adjusted R^2	.526	.521	.570
ΔR^2	.538**	.046	.076
F	43.108**	9.280**	7.293**

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. **p<.0005, *p=.03

Table 14

Hierarchical Multiple Regression on Receptive Language at Time Two

Variables	Step 1 Receptive Language at Time One	Step 2 Illness Severity & Familial Variables	Step 3 Interactions
ROWPVT Time 1	.504***	.404***	.370***
Viral load at Time 2		-.003	-.036
Adult-to-child ratio Time 1		.314**	.356**
# Caregivers lost to death Time 1		-.295	-.313
# Months since caregiver loss Time 1		.096	.127
Interaction ratio x viral load			.080
Interaction # caregivers x viral load			.159
Interaction # months x viral load			-.402**
Adjusted R^2	.233	.327	.382
ΔR^2	.254***	.162*	.097
F	12.575***	4.691***	3.938***

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. ***p≤.01, **p<.05, *p<.10

Table 15

Hierarchical Multiple Regression on Attention/Hyperactivity at Time Two

Variables	Step 1 Illness Severity & Familial Variables	Step 2 Interactions
Viral load at Time 2	.221	.148
Adult-to-child ratio Time 1	-.167	-.187
# Caregivers lost to death Time 1	-.257	-.280
# Months since caregiver loss Time 1	.131	.171
Interaction ratio x viral load		-.299*
Interaction # caregivers x viral load		-.054
Interaction # months x viral load		.094
Adjusted R^2	-.010	-.007
ΔR^2	.096	.082
F	.903	.962

Note. Excluding F, Adjusted R^2, and ΔR^2, scores are standardized partial regression coefficients (β) after each step. *p<.10

CHAPTER 4: DISCUSSION

The purpose of this study was two-fold. The first goal was to describe the extent to which intellectual and language functioning changed over time and/or differed across gender among HIV-infected children. Attention/hyperactivity functioning was also compared between males and females. The second goal was to expand upon cross-sectional studies that have found associations between home environmental variables and cognitive functioning of HIV-infected children. More specifically, the second study question examined the associations between illness severity (i.e., viral load at Time Two) and familial variables (i.e., Time One adult-to-child ratio in the home, number of caregivers the child has lost to death, number of months since the child has lost a caregiver to death) with intellectual, language, and attention/hyperactivity functioning at Time Two. The current study sample was demographically similar to the United Stated pediatric HIV population and, therefore, holds potential for increasing our knowledge of the families most affected by this illness.

The current sample was predominantly low SES, African-American, urban, children who were perinatally infected with HIV. The majority of the children was prenatally exposed to drugs, had mild to moderate clinical symptoms of HIV, had moderate to severe immune suppression, and was prescribed HAART for treatment of HIV. At the beginning of the study, 31% of participants had lost at least one caregiver to death, and the majority of children lived in homes with at most one other child and one or two adults.

Descriptive Summary

On average, the participants performed more than one standard deviation below the normative sample mean for the WISC-III and WPPSI-R on global, verbal, and performance IQ. Some previous research comparing HIV-infected children to non-infected children, seroreverters or the normative group identified the same global cognitive impairments in HIV-infected children (Belmann et al., 1988; Blanchette et al., 2001; Kullgren et al., 2004; Papola et al., 1994; Nozyce et al., 1994). However, two research groups found no global intellectual differences between HIV-infected and non-infected children, but both identified focal deficits specific to the HIV-infected group (Bisiacchi et al., 2000; Fishkin et al., 2000). Thus, the current research is consistent with studies demonstrating global (i.e., FSIQ) and more specific deficits (i.e., VIQ, PIQ) for HIV-infected children relative to normative samples, but inconsistent with studies finding no global intellectual deficits for HIV-infected children. There are three possible explanations for the discrepant findings in previous studies, and the discrepancy with respect to this sample compared to Bisiacchi et al. (2000) and Fishkin et al. (2000). One explanation is the introduction of HAART in 1996, resulting in improved functioning in the samples of more recent studies. Only 57% of the current sample received HAART at the first assessment point. A second possible explanation is the use of different reference groups (i.e., a control group, the normative reference group) across studies. When HIV-infected children are compared to national norms (i.e., the current sample; Bachanas et al., 1998; Cohen, 1994; Kullgren et al., 2004), the performance on global intellectual measures is indicative of problems. However, when HIV-infected children are compared to demographically similar children (e.g. Blanchette et al., 2002; Cohen et al., 1991), there tend not to be differences. The third potential explanation was also espoused by Kullgren et al. (2001) and relates to routes of HIV transmission.

Specifically, children in this sample performed similarly to other vertically-infected HIV-positive children (Brouwers, DeCarli et al., 1995; Havens et al., 1994; Papola et al., 1994; Tardieu et al., 1995), but poorer than transfusion-infected HIV-positive children (Browers et al., 1995; Cohen et al., 1991). At present, very few children contract HIV through transfusion, indicating that the performance of vertically-infected children is more representative of HIV-infected children as a whole.

It is important to note that the current sample is not only HIV-infected, they are also predominantly African-American. The current results are consistent with the mean IQ scores reported for African-American children as a group (Sattler, 1992). Havens et al. (1994) matched children on age, sex, race, foster care placement, and prenatal drug exposure, and found that HIV-infection is associated with poorer functioning on overall IQ. Therefore, one would expect African-American, HIV-infected children to perform lower than their Euro-American, non-infected counterparts and non-infected African-American peers. It is crucial to note that the Havens study was conducted prior to the advent of HAART. The use of HAART may be a protective factor and explain why the current sample of predominantly African-American HIV-infected children cannot be distinguished from non-infected Africa-American children with regard to their intellectual functioning.

At Time One, the group means were not considerably different from the normative sample mean on language functioning, with the exception of expressive language functioning. Specifically, at the first assessment point (not necessarily the first time the child had been exposed to this measure), the collective group performance fell more than one standard deviation below the normative sample only on the expressive language measure. However, 55% and 36% of the sample scored more than one standard deviation below the means on the EOWPVT and

ROWPVT, respectively. Thus, a large percentage of the current sample is evidencing some impairment in language abilities. Additionally, as seen in other studies (e.g., Wolters et al., 1994), expressive language is more impaired than receptive language.

Regarding attention/hyperactivity, the study participants' performances were no different than the normative sample participants' performance as a whole. Though consistent with Cohen et al.'s (1991) results, the majority of other previous research indicates that attention and/or hyperactivity are problem areas for HIV-infected children as compared to non-infected children or normative groups (Boivin et al., 1995; Brouwers et al., 1989; Brouwers et al., 1992; Hittleman et al., 1993). The Kullgren et al. (2004) study, which utilized children from this same population and clinic, reported that these children are at risk for behavioral problems. However, a more global measure of attention/hyperactivity was used in the present study, compared to several specific areas independently representing behavioral problems in the Kullgren et al. (2004) study, and the current results are consistent with other global measure findings of attention/hyperactivity disorders among HIV-infected children (i.e., Brouwers, Moss, & Poplack, 1992; Cohen et al., 1991; Havens et al., 1993; Whitt et al., 1993). Given the previous findings and the results of this study, examination of the clinical significance of children's ratings on the hyperactivity/ADHD index is warranted. In the current sample only five children (12%) scored in the clinical range at Time Two.

Cognitive Functioning Over Time and Between Genders

Mixed between-within subjects ANOVAs were utilized to answer the study question of how intellectual and language functioning is affected by time and/or gender. There was not a statistically significant difference between males and females over time for any of the intellectual outcomes. This is surprising because girls tend to perform better than boys on VIQ; and the

opposite is true for PIQ (Maccoby & Jacklin, 1974). The expected gender effect may not have appeared because of a small sample size, particularly for males (N=12). Consistent with previous research (Wolters et al., 1997), time did not have a significant effect on any of the intellectual outcomes. It is noteworthy, that the Wolters sample was similar to the current sample in that most were treated with antiretroviral medication during the study period. Though there was a slight improvement in the current sample's scores for FSIQ and PIQ over time, this change is not statistically or clinically significant and can most likely be explained by practice effects or the tendency for scores to regress toward the mean over repeated assessments. Moreover, IQ is typically relatively stable by age six years (Bloom, 1964; McCall et al., 1973); however, Loveland et al. (2000) demonstrated a decline in neuropsychological functioning in HIV-infected children which was associated with a decline in immune system functioning. By Time Two, the vast majority of children in this study were being treated with HAART and showed no worsening of HIV illness severity (as measured by viral load). In summary, these findings provide support for a positive impact of medication over time on intellectual functioning, perhaps due to arresting the progression of HIV illness severity and the commensurate decline in immune system functioning.

Regarding expressive language functioning, both males and females improved significantly in their expressive language functioning over time. In contrast, another longitudinal study regarding language functioning in HIV-infected children (Wolters et al., 1997) found that both receptive and expressive language functioning declined over time, despite antiretroviral therapy. However, none of the Wolters et al. (1997) sample received the newer protease inhibitors, rather they received nucleoside reverse transcriptase inhibitors. In contrast, by Time Two, 81% of the current sample was receiving HAART (which included a protease inhibitor)

and, thus, as a group were not evidencing greater illness severity over time. Specifically, the mean viral load of the current total sample improved over time. An earlier study by Wolters et al. (1995) revealed a significant relationship between greater severity of CT scan brain abnormalities and poorer language functioning in a sample of HIV-infected children. Thus, one might expect a decline in language abilities as well in the Wolters et al. 1997 sample, but not in the current one.

With regard to receptive language functioning, there also was a significant interaction between time and gender. Specifically, over time males' receptive language skills improved, and females' receptive language skills did not change significantly. Any gender difference in language functioning is surprising (Stoner & Spencer, 1983; Wiesner & Beer, 1991), but especially this opposite effect over time for boys and girls. Paired-samples t-tests revealed no significant difference between males (Time One m=3,872; Time Two m=10,379) and females (Time One m=9,331; Time Two m=6,363) on viral load at either assessment [Time One $t(40)=-1.523$, $p>.05$; Time Two $t(40)=.978$, $p>.05$). Therefore, this gender difference cannot be explained by viral load and may be better considered in the context of this effect of time for boys being based on a sample of only twelve boys.

Although changes in the attention/hyperactivity measurement tool prevented useful interpretation of any potentials changes in functioning over time, comparison between genders was accomplished. The hypothesis that males would have more attention/hyperactivity difficulties (Conners, 1990 and 1997) was not supported in this study. The lack of a significant finding may be due to the small sample size (males = 12, females = 30).

Hierarchical Multiple Regression Summary

Hierarchical regression analyses were used to determine the extent to which Time One family variables and Time Two illness severity affect intellectual, language, and attention/hyperactivity functioning at Time Two. The independent and interactive effects of these variables were examined. Prior to conducting the primary analyses, correlational analyses were conducted to explore relationships between demographic, medication, and predictor variables and Time Two outcome variables. Previous research tends to show an inverse relationship between illness severity or disease progression and the current outcome variables, such that sicker children perform worse on intellectual, language, and behavioral measures (Noyze et al., 1994; Pollack et al., 1996). Therefore, it is surprising that viral load was not significantly associated with any of the outcome variables in the current study. The restricted range of HIV illness severity, as measured by viral load in the current study, may explain the limited findings here. Specifically, in another study using viral load as the marker of illness severity (Pollack et al., 1996) a relationship was found between illness severity and cognitive functioning. However, there was more viral load range (<10,000 to 5,100,000) in the Pollack et al. 1996 sample than in the current study Time Two viral load variable (400 to 41,930). The restricted range of viral load in the present study as time progressed is certainly a positive observation. However, the range restriction also limits our ability to demonstrate relationships between illness severity and the outcome variables in the current study.

Regarding family predictor variables, there was only a significant relationship between the adult-to-child ratio and Time Two receptive language skills, such that as the number of adults to children increased so did the child's receptive language functioning. This finding was expected. However, given the implications of previous research (Rotheram-Borus et al., 1997;

Bachanas et al., 1998), the lack of correlation between number of deceased caregivers and the outcome variables is surprising. Further discussion of the lack of significant relationships between predictors and outcomes is presented below.

The total models for all three intellectual outcomes were significant in their explanation of Time Two functioning. However, only Time One intellectual functioning contributed significantly to the Time Two intellectual functioning models. This is a strong indication that for HIV-infected children, like other children, the best predictor of future cognitive performance is current/past cognitive performance. Neither the independent nor the interactive effects of illness severity and family variables significantly helped to explain a child's performance on measures of IQ at Time Two. The lack of significant family variables is inconsistent with the Kullgren et al.'s (2004) and Coscia et al.'s (2001) cross-sectional results, which found that home environment, or family variables were significantly associated with intellectual functioning. Furthermore, correlational analyses between Time One family variables and Time Two functioning, but not controlling for Time One functioning, were also not significant. This indicates that the influence of the measured family/home variables, although significant in a cross-sectional investigation, do not persist over time with regard to intellectual functioning. In addition to sample size, the lack of significant findings may be associated with the type of family variables examined. Perhaps a more fine-grained analysis of family factors (e.g., placement after caregiver death, parenting quality) would provide richer results.

As with intellectual functioning, Time One language functioning contributed significantly to the Time Two expressive and receptive language models, and the complete models explained a significant portion of the variance in Time Two language functioning. Again, past performance was more telling of future performance than is the presence of HIV, in this sample.

Familial and illness variables were not independently predictive of expressive language functioning at Time Two. However, adult-to-child ratio independently influenced Time Two receptive language functioning. The independent contribution of adult-to-child ratio was significant, while illness severity at Time Two was not; thereby indicating that with regard to receptive language functioning, this Time One family variable has more influence than current HIV illness severity. Specifically, as the number of adults per child in a home increased at Time One, there was an increase in the child's receptive language functioning at Time Two. This finding speaks to the contribution of adults in the home to receptive language functioning among HIV-infected African American children. Children with more adults in the home may be benefiting from a greater frequency of being read to and/or the more sophisticated verbal exchanges that tend to occur between adults relative to adult-child verbal exchanges. The cultural norm of kinship support for child-rearing within African American families may serve as a protective factor for HIV-infected children to the extent that it increases the likelihood of having more adults in the home.

The interaction between number of months since death of a caregiver and illness severity was predictive of both expressive and receptive language functioning at Time Two and the patterns were similar for both outcome variables. Specifically, among children who have not lost a caregiver, the more ill children evidenced better developed language skills (i.e., expressive and receptive). This finding is certainly counterintuitive, as one would expect children with higher viral loads to perform less well on tests of language development. Once again, the restricted range in viral load may play a role in this surprising finding. When a caregiver has been recently lost to death (i.e., less than two years), children tend to perform more similarly, regardless of viral load. Importantly, the children whose caregiver has recently died are scoring relatively low

on measures of language development (mean for expressive for both more ill and less ill group = 88; mean for receptive for both more ill and less ill group = 82), perhaps speaking to the negative impact of recent caregiver loss on functioning. However, it is also important to consider that only six children in this sample have recently lost a caregiver to death. With respect to the third group of children, those who lost a caregiver to death more than two years prior to the assessment, less ill children are performing better than their more ill peers. This finding is in the expected direction but, again, should be interpreted with caution given the small number of children falling into this group.

Finally, illness severity and familial variables together failed to significantly predict Time Two attention/hyperactivity functioning. With a larger sample size, the predictive variables used in this study may prove themselves to be useful in prediction of future attention/hyperactivity difficulties.

Limitations

While the current sample represents the pediatric population most affected by HIV, that is perinatally infected Southern, African-American children, these findings should not be generalized beyond those sample characteristics. For example, transfusion-infected or behaviorally-infected children of other ethnicities and from other geographic areas may differ in important ways from the current sample. The wide age range of study participants (3 – 12 years at Time One) is not ideal as we could not consider developmental stages within the small sample size. These patients had been accurately diagnosed with HIV and were being treated in an infectious disease clinic for at least one year by the time of the second assessment. Therefore, their results may not generalize to groups of children whose diagnosis has gone undetected and untreated for some time. Also, approximately half of the children in this sample were prenatally

exposed to drugs, but this information was not available for the entire sample and comparative analyses were not conducted to explore this factor. Finally, although the majority of patients were being treated with HAART, their pharmacologic treatment history was not accounted for in this study.

Measurement issues pose additional limitations to this study. With regard to the measurement of family variables, the number of months since caregiver death was not always known. Therefore, a uniform estimate was made for the middle of the known year of death. However, this variable posed multiple other problems conceptually. Caregivers, in this study, were defined as individuals with whom the child resides with for a significant portion of time and with whom the child was living or had a close relationship with at the time of caregiver death. However, most previous research regarding caregiver loss to death is specific to parental death, and the child has typically lived with that caregiver since birth, which is not necessarily the case in the current study. With regard to outcome measures, the change in attention/hyperactivity measurement tool during the study eliminated the possibility of examining the effect of time on this area of functioning and presents some limitations for the regression analyses.

There was also an important statistical limitation in this study. The sample size is reasonable given the population of interest and the need for longitudinal research questions; however, there is a resultant decrease in statistical power.

Implications

The results of the initial study question indicate that time and/or gender are more significant predictors of language functioning than of intellectual and attention/hyperactivity functioning in a sample of HIV-infected children. Expressive language functioning increased

over time for the entire sample, but females were clinically more impaired than males in this domain. Over time males' receptive language skills improved significantly and females' receptive language skills showed a declining trend. Equally as important was the finding that in a sample of children treated predominantly with HAART, intellectual functioning was stable over time. Taken together, these findings indicate that providers, educators, and families should not expect to see an overall pattern of decline in cognitive functioning in HIV-infected children over time when they are treated with HAART. Moreover, targeting language development through medical and educational strategies may be helpful.

The results of the longitudinal portion of this study offer limited support to important cross-sectional findings regarding the predictive power of family variables on functioning among HIV-infected children. This study offers some, though limited, support for inclusion of family and illness variables based on chronic illness theoretical models (Moos & Tsu, 1984; Thompson et al., 1994; Wallander & Varni, 1998) and Bronfenbrenner's Ecological Systems Theory (1979). In this sample, illness and family variables were not predictive of intellectual functioning at a later date. However, this study suggests that aspects of the child's current home environmental situation (i.e., adult-to-child ratio, time since loss of caregiver to death) are important in the understanding of future receptive language functioning. Kullgren et al. (2004) and Coscia et al. (2001) have found significant relationships between family/home environmental variables and intellectual functioning cross-sectionally. The current study seems to indicate that the influence of the family and home is stronger on future language functioning than intellectual functioning. Whereas intelligence is relatively fixed after age six, language development after this age is ongoing and influenced by the home environment. However, the restricted range of illness severity at Time Two (as measured by viral load) and the few participants falling into subgroups

for interpretation of interactions speak to a need for investigation of these variables in a larger and broader samples to fully appreciate the significant findings of this study. It is also speculated that a larger sample size would reveal significant relationships between family variables, illness severity, and attention/hyperactivity functioning over time. A clinical implication of these results is that family variables may be important in the long-term prediction of child functioning, even when compared to the predictive utility of current illness severity. Also, children who are more ill from HIV appear to need even more and lengthier support in recovering from the loss of a caregiver, than their healthier HIV-infected peers. The predictive utility of other family variables also should be explored, such as parenting style, number of geographical transitions, the relation of the caregiver to the child, or caregiver's level of education. These factors should be taken together to identify the risks and resources that may be influential to the child's functioning in the future. For example, interventions might target providing more resources to children across illness stages and as needed to enrich their given home environments.

Conclusions

HIV illness severity plays far less of a role in the prediction of future intellectual functioning than it has in the past. This study implies that the cognitive functioning of children on HAART is more influenced by family factors, than HIV illness severity. Future research should continue to explore the individual and additive influences of illness, medication, and family variables on intellectual language, and attention/hyperactivity functioning of HIV-infected children. Independent research is beginning to highlight a theme that family variables cannot be overlooked in their importance as protective resources for cognitive functioning of children living with HIV. These children and families are no longer facing a terminal illness,

rather they need resources and interventions to help them battle a chronic illness. Looking within the family, as well as to the medical field, we will increase our ability to provide high quality care to these children and families.

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