

Neurocognitive Disturbances in HIV-Infected Children with Viremia

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Abstract

Background: Children infected with HIV are at increased risk for developing central nervous system disease characterized by cognitive, language, motor, and behavioral impairments. Although HIV-infected children on HAART may have an overall cognitive functioning within normal limits with adequate functioning in school and activities of daily living, they often have significant impairments in selective neurobehavioral functions. We hypothesize that children with viremia (>400 copies HIV RNA/mL) will have evidence of decreased neurocognitive function compared with healthy, uninfected controls and infected children without viremia (<400 copies HIV RNA/mL).

Methods: Neurobehavioral testing was performed on 22 HIV-infected children and 20 controls (8-17 years) enrolled in an 18-month study. In the baseline analysis HIV-infected children were divided into those with (n=14) and without (n=8) viremia. Statistical methods: Kruskal-Wallis test and ANOVA.

Results: HIV-infected children with viremia performed 1.5 to 2 standard deviations below controls on all components of the Children's Paced-Serial Addition Test (p=0.01 to 0.08). Children with viremia also had lower scores than controls on the Delis-Kaplan Executive Function System motor speed assessment with mean scaled scores of 9.0 ± 3.0 and 11.25 ± 2.6, respectively (p=0.01). Parents of HIV-infected young children with viremia (n=6, 8-11 years) endorsed fewer symptoms of depressed mood (p=0.01) than did parents of controls (n=7) on the Behavior Assessment System for Children (BASC). There were no differences in parent-endorsed symptoms of depression among older children (12-17 years) on the BASC adolescent subscale.

Conclusions: HIV-infected children with viremia have significantly decreased attention and motor coordination compared with healthy controls. Parents of children with HIV may underestimate the impact of the infection on their child's mental health, a phenomenon described in other chronic diseases.

Introduction

Children infected with HIV are at increased risk for developing central nervous system (CNS) disease characterized by cognitive, language, motor, and behavioral impairments. The severity of HIV-related CNS manifestations in children range on a continuum from subtle impairments in selective domains to severe deterioration of global developmental skills. HIV-related CNS dysfunction in children is primarily the result of HIV infection in the brain. Various neurotoxic factors released by the virus and host cells are postulated as the main causes of neurologic dysfunction and damage. Children exhibit CNS disease more frequently than adults, and may develop CNS complications several years after infection. The decline in the prevalence of severe HIV-related CNS manifestations may be related in part to the earlier and more generalized use of combination antiretroviral treatment (ART), including HAART. The CNS may serve as a reservoir for persistent HIV infection however, as many antiretroviral agents, including protease inhibitors, do not penetrate well into this compartment.

With the widespread availability of HAART, children displaying CNS disease are more likely to exhibit HIV-related CNS compromise, rather than the encephalopathy frequently seen during the first decade of the AIDS epidemic. Our studies have shown that this CNS compromise is defined by an overall cognitive functioning that is within normal limits and continued adequate functioning in school and activities of daily living, but with significant impairments in selective neurobehavioral functions. The purpose of this study was to further characterize the neurocognitive deficits associated with HIV disease progression in the pediatric population.

Methods

Study Population: Two groups of children were enrolled in this study, the subject group of 29 children, ages 8-17 with HIV infection, and the control group of 33 HIV exposed, HIV uninfected children, ages 8-17 years.

Study Overview: The study and control subjects were admitted for 24 hours to the General Clinical Research Center at Texas Children's Hospital. During these visits, all participants underwent neurocognitive and psychological testing. HIV disease progression markers were obtained in the HIV-infected subjects.

Neurobehavioral Test Battery: A number of tests were utilized in the neurobehavioral assessment of study and control subjects during the GCRC admission to evaluate intelligence, attention, fatigue, and memory. Subjects and their parents also completed questionnaires assessing behavior, depression, anxiety, and other activities affected by sleep disturbances or fatigue.

Statistical Methods: The T-test and Kruskal-Wallis test were used to compare the neurobehavioral test results of the HIV-infected subjects to controls. Significant differences resulting from the Kruskal-Wallis test in the 3-group analysis (controls vs. HIV-infected children with/without viremia) were further evaluated with a multiple comparisons test.

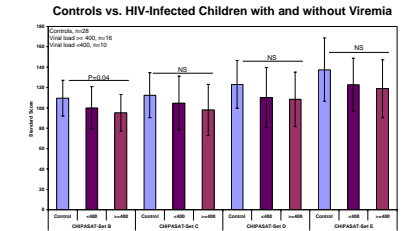
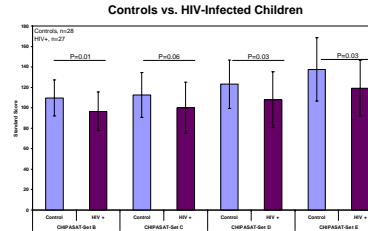
Results

Demographics

	HIV-Infected Children	Controls
Number	29	33
Mean age, years (range)	12.8 (8-17)	12.6 (8-17)
Gender, M/F		
Female (number)	55% (16)	48% (16)
Male (number)	45% (17)	52% (17)
Race (number)		
African American	76% (22)	78% (25)
Caucasian	17% (5)	16% (5)
Other	7% (2)	6% (2)
Latino Ethnicity (number)	11% (3)	15% (5)
Family Income (number)		
\$10,000 or less	26% (7)	28% (8)
\$10,001-40,000	63% (17)	55% (16)
>\$40,000	11% (3)	17% (5)

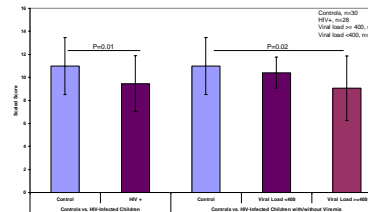
There were no significant demographic differences between the HIV-infected subjects and the controls. There were also no differences between the 18 HIV-infected children with viremia (viral load >400 copies/ml) and the 10 children with undetectable viral loads (<400 copies/ml, data not shown).

Children's Paced Auditory Serial Addition Test

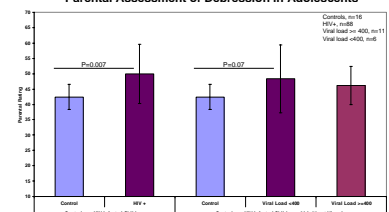


HIV-infected subjects on average performed one standard deviation lower than controls on the PASAT, an auditory serial addition test requiring intense concentration. Children with viremia had lower scores than children with undetectable viral loads. Error bars represent the standard deviations.

Delis-Kaplan Motor Speed Assessment



Parental Assessment of Depression in Adolescents



HIV-infected children had decreased motor speed compared to controls. The children with viremia were slower than children without viremia. On the Behavior Assessment System for Children adolescent depression subscale, adolescents with HIV were reported to be less depressed than controls by their parent/guardian.

Discussion and Conclusions

Children with HIV-infection appear to have significant deficits in attentional processing and motor speed as compared to controls. We observed that these problems were even more pronounced in children with viremia. Thus, it appears that HIV infection plays a role in disturbances of attention and motor coordination, especially in children with poorly controlled disease. It also seems that parents may underestimate the psychological impact of HIV infection on the mental health of their adolescent children. Since 50 percent of annual new infections with HIV (20,000 in the United States) occur in youth between 13 and 25 years, the magnitude of abnormal neurocognitive and psychosocial function should not be understated. In this growing number of youth and young adults, it is important to study the effects of HAART treatment on neurocognitive and psychosocial function. This study is a first step in approaching the gap that exists in understanding the impact of HIV disease on higher cortical function in children.

Support

Funded by grants from the National Heart, Lung, and Blood Institute, NIH (HL-079533), General Clinical Research Center (RR-0188) and Center for AIDS Research (AI-36211).