Brief Report: Relationship Between HIV Infection and WPPSI-R Performance in Preschool-Age Children

Peter E. Fishkin,1 MS, F. Daniel Armstrong,2 PhD, Donald K. Routh,1 PhD, Lynnette Harris,2 PhD, Winsome Thompson,1 MS, Katya Miloslavich,2 MS, Jacqueline D. Levy,1 MS, Arnise Johnson,2 MS, Connie Morrow,2 PhD, Emmalee S. Bandstra,2 MD, Craig A. Mason,1 PhD, and Gwendolyn Scott,2 MD
1University of Miami and 2University of Miami School of Medicine

Objective: To determine the neurodevelopmental effects of perinatally acquired HIV infection on children of preschool age.

Methods: Participants included 40 children infected with HIV between the ages of three and five and an equal number of noninfected controls individually matched according to ethnicity, age, sex, and prenatal drug exposure. Participants were administered the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), upon which an analysis of subtest distribution was conducted.

Results: Whereas both groups evidenced mean IQ and subtest scores significantly below published norms, an effect for HIV group status was not found when a factor combining Performance IQ (PIQ) and Verbal IQ (VIQ) was analyzed. However, the group infected with HIV scored significantly lower than controls on the Block Design subtest.

Conclusions: Gross cognitive deficits are not evident among preschool children infected with HIV relative to matched controls. However, this study does provide some evidence for more focal deficits. Further investigation with older children should be conducted.

Key words: human immunodeficiency virus (HIV); child development; neuropsychology.

Seventy-nine percent of children perinatally infected with HIV remain asymptomatic for several years (mean of 6.1 years until the development of AIDS); have a slow, progressive course; and survive up to 12 years or longer (Persaud et al., 1992). However, they often develop a specific pattern of neural deficits, including cerebral atrophy, especially myelinopathy of the prefrontal cortex, pyramidal tract signs, and calcification of the basal ganglia, as seen by computed tomography (CT), magnetic resonance imaging (MRI), and postmortem autopsy (Armstrong, Seidel, & Swales, 1993; Grattan-Smith, Harrison, & Singleton, 1992). These neurological deficits have been associated with several patterns of dysfunction, including intellectual decline, loss of developmental milestones, and changes in muscle tone (Armstrong et al., 1993; Belman, 1990; Brouwers et al., 1995).

This study examined the effects of HIV infection...
on the neurodevelopment of children between the ages of 3 and 5 years. We predicted that they would present a specific pattern of neurodevelopmental deficits consistent with Rourke's (1989) model of Nonverbal Learning Disability (NLD). Rourke has theorized that myelinopathy produces a syndrome (NLD), which includes impairments in nonverbal problem solving, mathematical skills, visual-spatial abilities, and adaptation to novel situations. As the children in this study were presumed to be infected relatively late in their neuronal development, these deficits, if they exist, are believed to be attributed to inhibited myelin formation and associated fiber development in late developing structures such as the prefrontal lobes. Significant deficits between preschool children infected with HIV and matched, healthy controls were expected in the following five subtests of the Wechsler Primary and Preschool Scale of Intelligence-Revised (WPPSI-R) (Wechsler, 1989): Animal Pegs, Block Design, Object Assembly, Arithmetic, and Mazes. These tasks require a variety of learning, perceptual, and motor skills for which normal development of the association and motor areas of the brain is necessary.

**Method**

**Participants**

The study sample was composed of 40 children, ages 3 to 5 years, infected with HIV, of African American (18) and Haitian (22) origin, who were tested as part of a clinical service project (Armstrong et al., 1999). These children are representative of the ethnic and socioeconomic level of the larger population of children treated for HIV. National statistics demonstrate that women and children of ethnic minority groups account for the fastest growing population infected with HIV (Centers for Disease Control and Prevention [CDC], 1997). The medical charts of the participants were reviewed to retrospectively determine the disease status of the child at the time of cognitive testing. Twenty-one children had illnesses consistent with a diagnosis of AIDS, eight had experienced AIDS symptomatology but did not meet criteria for a diagnosis of AIDS, and eight were HIV-positive and asymptomatic. Medical records were not available for three participants. At the time of this report, 13 of the original 40 children recruited for the study had died of AIDS-related complications. An equal number (40) of children who were control participants in other clinical studies, or who were healthy patients seen for well-child care at the medical center, were recruited as a comparison group. These children were not HIV-infected, had no other known chronic illness, had no history of congenital or acquired brain impairment or cognitive impairment. Participants in the control group were individually matched with the children in the HIV-infected group on as many variables as possible (i.e., age, ethnicity, gender, and prenatal drug exposure).

**Design and Procedure**

Informed consent to use the data from the clinical evaluation using the WPPSI-R was obtained from all participants who were living with their parents. A special procedure was employed in the remaining cases. This procedure, approved by the Institutional Review Board for the Protection of Human Subjects, was used in cases where children had died or were in state custody, or the parents had died. Relevant medical and demographic data were obtained by a research assistant who conducted a chart review and was blind to the performance on the WPPSI-R.

Data for this study were collected from five types of sources. Participant data were obtained from historic files of children infected with HIV who were evaluated as part of an ongoing study of neurodevelopment in children with HIV or as part of a clinical service program that involves annual evaluation of all children provided medical care for HIV infection at our center (see Armstrong et al., 1999, for a complete description of the program). Data for control group participants were obtained from historic files of children not infected with HIV who were healthy control participants for other clinical research studies, or were recruited for this study from well-child care settings.

**Results**

**Preliminary Analyses**

Cognitive impairments were evidenced by mean IQ and subtest scores for both participants infected with HIV and participants in control groups. As can be seen in Table I, mean FSIQ, PIQ, and VIQ scores for both groups were more than one standard deviation below WPPSI-R standardized sample norms. Subtest means for both groups were all more than 2 points lower than WPPSI-R group norms.
As expected, no significant differences were found between groups on any matching variable: Age: \( t(78) = -0.42, p = 0.68 \); Drug Exposure: \( t(78) = 0.24, p = 0.81 \); Ethnicity: \( t(78) = 0.00, p = 1.00 \); Gender: \( t(78) = 0.44, p = 0.66 \).

An overall effect for HIV group status was not found when a MANOVA was conducted for FSIQ, PIQ, and VIQ, \( F(1, 39) = 1.94, p = 0.172 \). On the other hand, an overall effect for test type was found, \( F(78, 2) = 16.84, p < 0.01 \). The combined HIV infection group and control group PIQ scores (means = 78.8, 82.9, respectively) were significantly higher than their combined VIQ scores (means = 72.6, 76.0, respectively) and their combined FSIQ scores (means = 73.2, 76.9, respectively). In order to determine whether the overall lack of significant difference was also true of each of the three scaled scores, individual \( t \) tests for FSIQ, PIQ, and VIQ were performed. Significant differences were not found between groups on any of the scaled IQ functions: FSIQ: \( t(39) = 1.30, p = 0.20 \); PIQ: \( t(39) = 1.30, p = 0.20 \); VIQ: \( t(39) = 1.32, p = 0.20 \).

There was no trend toward scores for control participants exceeding scores of participants infected with HIV. A sign test revealed that approximately half of the participants obtained a higher PIQ score than their matched controls (\( z = -0.16, p = 0.87 \)). The same was found to be true of VIQ scores (\( z = 0.00, p = 1.00 \)). Controls scored higher than their matched participant infected with HIV on FSIQ in only three out of every five pairs (\( z = -0.81, p = 0.42 \)). Individual \( t \) tests were performed to determine the pattern of differences for those subtests predicted to differ significantly between participants who were infected with HIV and those who were controls. A significant difference was only found for Block Design, \( t(39) = 2.47, p < 0.02 \). No significant differences were found between groups for those subtests on which the groups were predicted not to differ.

### Discussion

Our original hypothesis was that a pattern of deficits related to Rourke’s model of nonverbal learning disabilities (1989) would be found. This hypothesis was based on neuroimaging data from other studies that support significant changes in the frontal and prefrontal areas of the brain in children with perinatally acquired HIV infection. We did not find differences in the expected measures of frontal functioning, but a significant difference was found for Block Design, a complex task not usually considered a primary measure of frontal cortex functioning (Spreen & Strauss, 1998).

There are several potential explanations for this pattern of findings. First, Rourke’s NLD model is based primarily on children who are school-age or older, and it is possible that the functional deficits seen in these children are not developmentally present in the preschool children included in this study (Armstrong & Horn, 1995). Second, the subtests of the WPPSI-R, as well as other tests for preschool children, may not be the most sensitive and specific tests of frontal functioning and may not have been able to detect changes in the preschool child (Batchelor, 1996). Finally, the identification of differences in Block Design, a test sometimes associated with parietal lobe development (Spreen & Strauss, 1998), presents an unexpected finding, particularly since MRI and CT changes in the parietal area in the brains of children with HIV have not been reported, while frontal involvement is common. However, Block Design is a complex task that involves processing speed, visual motor integration, sustained attention, and motor speed and coordination. These functions are usually associated with the frontal cortex and developing connecting structures and are the ones that we originally hypothesized to be impaired in children with HIV (Armstrong et al., 1993). One possibility to be further explored is that differences in separate functions (e.g., visual-motor

### Table 1. WPPSI-R IQ and Subtest Scale Scores for Children With and Without HIV Infection

<table>
<thead>
<tr>
<th>Scale/Subtest</th>
<th>HIV-infected participants</th>
<th>Controls (noninfected)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( M )</td>
<td>(SD)</td>
</tr>
<tr>
<td>FSIQ</td>
<td>73.15</td>
<td>(13.86)</td>
</tr>
<tr>
<td>PIQ</td>
<td>78.80</td>
<td>(15.57)</td>
</tr>
<tr>
<td>VIQ</td>
<td>72.58</td>
<td>(12.62)</td>
</tr>
<tr>
<td>Block Design(^a)</td>
<td>6.08</td>
<td>(2.80)</td>
</tr>
<tr>
<td>Animal Pegs</td>
<td>6.78</td>
<td>(2.54)</td>
</tr>
<tr>
<td>Object Assembly</td>
<td>6.23</td>
<td>(3.27)</td>
</tr>
<tr>
<td>Arithmetic</td>
<td>5.85</td>
<td>(3.16)</td>
</tr>
<tr>
<td>Mazes</td>
<td>7.00</td>
<td>(3.52)</td>
</tr>
<tr>
<td>Information</td>
<td>5.03</td>
<td>(2.29)</td>
</tr>
<tr>
<td>Comprehension</td>
<td>5.38</td>
<td>(2.62)</td>
</tr>
<tr>
<td>Vocabulary</td>
<td>5.43</td>
<td>(2.69)</td>
</tr>
<tr>
<td>Sentences</td>
<td>7.83</td>
<td>(2.67)</td>
</tr>
</tbody>
</table>

\(^a\)The difference between the two groups was in the expected direction and was significant, \( p < .02 \).

WPPSI-R = Wechsler Preschool and Primary Scale of Intelligence, Revised; FSIQ = Full Scale Intelligence Quotient; PIQ = Performance Intelligence Quotient; VIQ = Verbal Intelligence Quotient.
integration, processing speed, sustained attention) are not detectable in preschool children using the subtests of the WPPSI-R, whereas more complex tasks that simultaneously involve a number of these functions, such as Block Design, may lead to significant results.

Several factors are known to affect outcomes on studies of cognitive functioning in children. Children with HIV are primarily from minority and low socioeconomic status (SES) populations (Centers for Disease Control and Prevention, 1997), and this sample also included some children who were bilingual. In this study, these factors were addressed by matching participants with HIV with control participants on these variables.

This study indicates that among the group of children infected with HIV who do not show severe infection effects soon after birth, cognitive development is comparable to that of peers from similar backgrounds through age five. This may not be true of older children infected with HIV. The children in this older group have a strong likelihood of developing greater cognitive deficits as the disease progresses. This presents another urgent reason for early detection and treatment of HIV infection in children. Appropriate, early treatment could benefit both the individual lives of these children and their families while substantially cutting the expense of educating these children by reducing the need for special education services.

As HIV shifts from a life-threatening disease to a chronic disease with long-term developmental consequences, our need to understand the neurodevelopmental effects of HIV increases. This study provides a snapshot of the specific pattern of neurological deficits found in asymptomatic preschool children infected with HIV. Recognizing the limited effect of the disease on asymptomatic children in this age range provides a window of opportunity for preventive intervention. It can also improve our ability to prepare for the needs of these populations and provide the most appropriate interventions for their future well-being if later problems are identified.

**Acknowledgments**

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