Cognitive Deficits in HIV Infected Children

O. S. Ravindran, Mrudula P. Rani¹, G. Priya¹

ABSTRACT

**Background and Objectives:** Children infected with HIV are at risk for significant neurological and neuropsychological problems. This study is aimed at identifying cognitive deficits in HIV-infected children and to compare them with equal number of normal controls. **Materials and Methods:** Twenty children with HIV infection who are currently on antiretroviral therapy were recruited. They were assessed for their intelligence using Malin's Intelligence Scale for Indian Children and also evaluated for their cognitive abilities with a comprehensive neuropsychological battery. They were matched with equal number of normal controls. **Results:** HIV-infected children have shown substantial impairments in the domains of attention, language, verbal learning and memory, visuomotor functions, fine motor performance, and executive functions. **Conclusion:** HIV-infected children have average intelligence, but they performed poorly on several neuropsychological measures.

**Key words:** Cognitive deficits, HIV infection, neuropsychological testing

INTRODUCTION

HIV is a fatal, sexually transmitted, or blood-borne disease affecting the health, cognitive abilities, and general well-being of the individuals including children and adolescents in particular. Children infected with HIV are at risk for significant neurological and neuropsychological problems. Neurological and cognitive deficits have been documented in up to 80% of HIV-infected children.¹ Development delays and neurologic complications, such as encephalopathy, have been identified in children who are infected with HIV since the earliest descriptions of the disease.²,³

HIV infects a variety of cell types in the brain leading to damage of the central nervous system (CNS).⁴ Neuropsychological tests serve as indirect measures to assess CNS functioning along with the more direct measures such as computed tomography and magnetic resonance imaging scans. Studies of HIV-infected children have reported that cognitive deficits are observed in the areas of language and motor skills,⁵,⁶ verbal and memory functioning,⁷ visual-spatial integrative ability,⁸,⁹ and executive functions.¹⁰

The recent development of highly active antiretroviral therapy (ART) has dramatically prolonged the survival of HIV-infected children. As HIV disease has moved from being a fatal to a chronic illness, cognitive, neurologic, and behavioral functioning of HIV-infected children has become a major concern. To date, not much studies of neuropsychological functioning of HIV-infected children who receive ART has been done in India.

MATERIALS AND METHODS

**Participants**

The sample for the present study comprised of 20 HIV-infected children who are inmates of a home exclusively for HIV-infected children in Chennai. The home which is run by a NGO is a special center, where they take care of HIV-infected children who belonged to low socioeconomic background. Majority of the parents
of these children are alive and 80% of them visit their children once in 3 months. There were 30 inmates in the home. After obtaining prior permission for the home authorities, all the parents and the local guardians of the inmates were contacted and the written informed consent was obtained from them after explaining the purpose of the study. All the children in the HIV-infected group were assessed individually for their intelligence using Malin’s Intelligence scale for Indian Children (II). The inclusion criteria were (a) Diagnosis of HIV infection made by the physician, which was confirmed with laboratory tests for HIV, (b) children who are receiving ART, (c) children up to 12 years of age of both sexes, (d) children with HIV infection through maternal transmission, and (e) children with an intelligence quotient (IQ) of 90 and above. The exclusion criteria were Children with a history of severe developmental disorder (e.g., autism) or significant psychiatric disorder or comorbid medical disorder not related to HIV. Out of 30, 20 HIV-infected children who fulfilled the inclusion and exclusion criteria were included in the study group.

Children with an IQ of 90 and above were only included in the study, because HIV infection affects the brain development in young children and causing intellectual deterioration. The children with HIV infection were matched with equal number of normal controls through purposive sampling. The subjects of the control group were selected from the schools in Chennai after obtaining permission from the school authorities and the written informed consent was obtained from the parents after the purpose of the study was explained to them. The children in the control group who had history of medical, psychiatric, or neurological disorders such as epilepsy that would affect the brain were excluded. They were also assessed for their intelligence individually after the class hours. Those who have obtained an IQ of 90 and above were included in the control group.

Procedure
All the children in both the groups were evaluated for their cognitive functions using a comprehensive neuropsychological battery.[11] The battery includes nine neuropsychological tests, which measures nine neuropsychological domains namely attention, language, visual memory, verbal learning and memory, visuo perceptual functions, visuospatial functions, visuomotor functions, fine motor performance, and executive functions. Each domain consists of one test only. These tests have been used by various authors[12,13] for assessing various neuropsychological functions and found to be sensitive. The tests were administered according to standard procedure given in the manual in two sessions over a period of 2 consecutive days. The duration of each session was 2 h. The tests selected for assessing the cognitive functions are as follows:

I. Attention
   Digit span (MISIC)
II. Language Vocabulary (MISIC)
III. Visual memory
   Benton Visual Retention Test
IV. Verbal learning and memory
   Rey Auditory Verbal Learning Test
V. Visuo perceptual functions
   Picture completion (MISIC)
VI. Visuospatial functions
   Block design (MISIC)
VII. Visuomotor functions
   Object assembly (MISIC)
VIII. Fine motor performance Coding (MISIC)
IX. Executive functions
   Trail making test (Part-B).

RESULTS
The sociodemographic characteristics of the participants are presented in Table 1. A total of 45% were in the age group of 8-9 years, while 55% were in the age group of 10-12 years in both HIV-infected and HIV-unexposed groups. Girls were 60% and boys were 40% in both the groups. In terms of educational level, 90% versus 60% in primary and 10% versus 40% were studying in secondary school. Regarding the status of HIV+, 85% of both father and mother were infected with HIV. All the HIV-infected children were under the care of home authorities, whereas all the children in the HIV-unexposed group were under the care of their parents. Parental education, age, and family income were lower in children with HIV infection than those in the control group and the details are presented in Table 2. Clinical status of HIV-infected children: All the children are taking ART for 2 years with a good adherence and they are nutritionally adequate at the time of induction into the study.

The neuropsychological evaluation findings of the two groups are presented in Table 3. The t-test was used to find out the difference between the means. The t-test indicated significant group differences on the measures of attention, language, verbal learning and memory, visuomotor functions, fine motor performance, executive functions but not on visual memory, visuo perceptual, and visuospatial functions. Comparison of scores for the two groups revealed that the HIV-infected group was more impaired on several neuropsychological measures than the control group.

DISCUSSION
Children with HIV infection are at high-risk for developing neurodevelopment and cognitive impairments.[14] Several studies have demonstrated neurodevelopmental
impairment among HIV-infected children as early as in infancy,[15,16] while other studies have demonstrated a neurocognitive deficit in HIV-infected preschool[17,18] and school-aged children.[19,20] Our study demonstrated that HIV-infected children have a mean IQ of 96 which was in the average range (the mean IQ of control group was 103) and this finding is similar to other studies.[21,22] However, they performed poorly on several neuropsychological measures such as attention,[23] language,[24] verbal learning and memory,[25] visuomotor functions,[26] fine motor performance,[27] and executive functions[28] when compared with control group.

The poor neurocognitive functions in HIV-infected children might be explained by the following reasons. First, HIV infection may have a direct effect on neurodevelopment during the first few years of life, which is the time of rapid brain development occurs or it may have an indirect effect through recurrent infections or opportunistic, leading to poorer general health. A Tanzanian study of HIV-infected infants reported that infants with in utero infection had higher risk of delayed mental functioning compared to infants who were diagnosed at a later stage of life.[16] Another factor that might contribute to poor neurocognitive outcome may be due to low socioeconomic background of HIV-infected children which could lead to a variety of obstacles such as inadequate food and lack of time for cognitively stimulating activities may have negative impact on the neurocognitive development. Environmental factors such as low level of maternal education, changes in care givers, and poverty which are likely to affect HIV-infected children adversely. Many studies[18,29,30] have observed that poverty and low socioeconomic status have been linked to poor outcomes on neurocognitive testing and similar findings are observed in the present study also.

Family structure and child rearing plays an important role in the neurodevelopment of the child. In our study, all the HIV-infected children are under the care of home authorities due to poverty in their families, while the normal controls lived with their parents. This finding is similar to a U. S. study, which reported that children living with their biological parents were less likely to manifest conduct or learning problems when compared to those living with others.[31]

In our study, the cognitive functions among HIV-infected children were impaired despite they received the ART for 2 years with undetectable viral load and normal CD4 cell. This is similar to a South African study which reported that HIV-infected children with a median age of 5 years were not shown improvement in neurocognitive functions after 6 months of ART.[18] Another study has also shown that neurocognitive functions do not improve with ART.[24]

**Implications of the study**

This is the first study from this part of the country to assess the neurocognitive status of HIV-infected children. The findings in this study indicate that the

Table 1: Sociodemographic variables of the participants

| Variables                | Group 1 (n (%)) | Group 2 (n (%)) |
|--------------------------|----------------|----------------|
| Age (years)              |                |                |
| 8-9                      | 9 (45)         | 9 (45)         |
| 10-12                    | 11 (55)        | 11 (55)        |
| Gender                   |                |                |
| Boys                     | 8 (40)         | 8 (40)         |
| Girls                    | 12 (60)        | 12 (60)        |
| Education                |                |                |
| Primary                  | 18 (90)        | 12 (60)        |
| Secondary                | 2 (10)         | 8 (40)         |
| Status of HIV+           |                |                |
| Both parents             | -              | -              |
| Only mother              | -              | -              |
| Only father              | -              | -              |

Table 2: Family characteristics of the two groups

| Variables          | Group 1 | Group 2 |
|--------------------|---------|---------|
| Mean age (years)   |         |         |
| Father             | 30      | 33      |
| Mother             | 26      | 28      |
| Father’s education |         |         |
| None               | 4 (20)  | 5 (25)  |
| Primary            | 10 (50) | 11 (55) |
| Secondary          | 6 (30)  | 4 (20)  |
| Higher secondary   | -       | -       |
| Mother’s education |         |         |
| None               | 6 (30)  | -       |
| Primary            | 14 (70) | 5 (25)  |
| Secondary          | -       | 12 (60) |
| Higher secondary   | -       | 3 (15)  |
| Income (in Rupees) |         |         |
| Upto 5000          | 15 (75) | 3 (15)  |
| 5001 to 7000       | 5 (25)  | 10 (50) |
| 7001 and above     | -       | 7 (35)  |

Table 3: Neuropsychological test findings of the two groups

| Cognitive domain                | Group 1 (n=20) | Group 2 (n=20) | t   |
|---------------------------------|---------------|---------------|-----|
| Attention                       | Mean          | SD            | Mean | SD | 3.63** |
|                                 | 7.85          | 1.22          | 9.25 | 1.20 |
| Language                        | Mean          | SD            | Mean | SD | 4.91** |
|                                 | 21.70         | 5.30          | 30.30| 5.75|
| Visual memory                   | Mean          | SD            | Mean | SD | 1.41 |
|                                 | 6.60          | 1.14          | 7.30 | 1.41 |
| Verbal learning and memory      | Mean          | SD            | Mean | SD | 2.07* |
|                                 | 44.05         | 0.36          | 50.95| 0.62|
| Visuoperceptual functions       | Mean          | SD            | Mean | SD | 2.13 |
|                                 | 8.35          | 2.09          | 8.75 | 2.13|
| Visuospatial functions          | Mean          | SD            | Mean | SD | 1.02 |
|                                 | 14.60         | 7.29          | 14.95| 8.63|
| Visuomotor functions            | Mean          | SD            | Mean | SD | 2.29* |
|                                 | 8.60          | 3.15          | 11.30| 4.23|
| Fine motor performance          | Mean          | SD            | Mean | SD | 4.58** |
|                                 | 33.25         | 6.54          | 42.95| 6.84|
| Executive functions             | Mean          | SD            | Mean | SD | 0.91 |
|                                 | 2.50          | 1.73          | 1.25 | 0.91|

*P<05, **P<01; SD – Standard deviation
Cognitive deficits have been observed in the domains of attention, language, verbal learning and memory, visuomotor functions, fine motor performance, and executive functions.

ACKNOWLEDGMENT

The authors would like to acknowledge Dr. M. S. Karthick, Assistant professor of Psychiatry for his suggestions in manuscript preparation.

REFERENCES

1. Tahan TT, Bruck I, Burger M, Cruz CR. Neurological profile and neurodevelopment of 88 children infected with HIV and serooverter children followed from 1995 to 2002. British J Infect Dis 2006;10:322-6.
2. Knight WG, Mellins CA, Levenson RL Jr, Arbadi SM, Kairam R. Brief report: Effects of ediatric HIV infection on mental and psychomotor development. J Pediatr Psychol 2000;25:583-7.
3. Nozyce M, Hitteljan M, Muenz L, Durako SJ, Fischer ML, Willoughby A. Effect of perinatally acquired human immunodeficiency virus infection on neurodevelopment in children during the first years of life. Pediatrics 1994;94:883-91.
4. Gartner S. HIV Infection and dementia. Science 2000;287:602-4.
5. Condini A, Axia G, Cattelan C, D’Urso MR, Laverda AM, Viero F, et al. Development of language in 18-30-month-old HIV-1-infected but not ill children. AIDS 1991;5:735-9.
6. Drotar D, Olness K, Wiznitzer M, Guay L, Marum L, Svilas G, et al. Neurodevelopmental outcomes of Ugandan infants with human immunodeficiency virus type infection. Pediatrics 1997;100:E5. Available from: www.pediatrics. org/cgi/content/full/100/1/e5. [Last accessed on 1997].
7. Levenson RL, Mellins CA, Zawadzki R, Stein Z. Cognitive assessment of human immunodeficiency virus-exposed children. Am J Dis Child 1992;146:1479-83.
8. Boivin MJ, Green SD, Davies AG, Giordani B, Mokili JK, Cutting WA. A preliminary evaluation of the cognitive and motor effects of pediatric HIV infection in Zairian children. Health Psychol 1995;14:13-21.
9. Diamond GW, Gurdin P, Wizin AA, Belman AL, Rubinstein A, Cohen HJ. Effects of congenital HIV infection on neurodevelopmental status of babies in foster care. Dev Med Child Neurol 1990;32:999-1004.
10. Bisicacchi PS, Suppiej A, Laverda A. Neuropsychological evaluation of neurologically asymptomatic HIV-infected children. Brain Cogn 2000;43:49-52.
11. Malin AJ. Malin’s intelligence scale for Indian children. Indian Journal of Mental Retardation;1971;4:15-25.
12. Fundaro C, Miccinesi N, Baldieri NF, Genoveso G, Rendeli C, Segni G. Cognitive impairment in school-age children with asymptomatic HIV infection. AIDS Patient Care STDS 1998;12:135-40.
13. Loveland KA, Stehbins JA, Mahoney EM, Siros PA, Nichols S, Bordeaux JD, et al. Declining immune function in children and adolescents with hemophilia and HIV-infection: Effects on neuropsychological performance. Hemophilia Growth and Development Study. J Pediatr Psychol 2000;25:309-22.
14. Willen EJ. Neurocognitive outcomes in pediatric HIV. Ment Retard Dev Disabil Res Rev 2006;12:223-8.
15. Louthrenoo O, Puthanakit T, Wongnum N. Early neurodevelopment of infants born to HIV-seropositive mothers. Chiang Mai Med Bull 2004;43:1-7.
16. McGrath N, Fawzi WW, Bellinger D, Robins J, Masamaga GI, Manji K, et al. The timing of mother-to-child transmission of human immunodeficiency virus infection and the neurodevelopment of children in Tanzania. Pediatr Infect Dis J 2006;25:47-52.
17. Fishkin PE, Armstrong FD, Routy DK, Harris L, Thompson W, Milelavich K, et al. Brief report: Relationship between HIV infection and WPPSI-R performance in preschool-age children. J Pediatr Psychol 2000;25:347-51.
18. Smith L, Adams C, Eley B. Neurological and neurocognitive function of HIV-infected children commenced on antiretroviral therapy. S Afr J Child Health 2008;2:108-13.
19. Koekkoek S, de Sonneville LM, Wolfs TF, Licht R, Geelen SP. Neurocognitive function profile in HIV-infected school-age children. Eur J Paediatr Neurol 2006;10:336-79.
20. Trudie M, Mayaux MJ, Seibel N, Funck-Brentano I, Straub E, Teglas JF, et al. Cognitive assessment of school-age children infected with maternally transmitted human immunodeficiency virus type 1. J Pediatr 1995;126:375-9.
21. Bagenda D, Nasalai K, Kalyesubula I, Sherman B, Drotar D, Boivin MJ, et al. Health, neurologic, and cognitive status of HIV-infected, long-surviving, and antiretroviral naive Ugandan children. Pediatrics 2006;117:729-40.
22. Loveland KA, Stehbins JA, Contant C, Bordeaux JD, Siros P, Bell TS, et al. Hemophilia growth and development study: Baseline neuropsychological findings. J Pediatr Psychol 1994;19:223-39.
23. Brackis-Cott E, Kang E, Dolezal C, Abrams EJ, Mellins CA. The impact of perinatal HIV infection on older school-aged children’s and adolescents’ receptive language and word recognition skills. AIDS Patient Care STDS 2009;23:415-21.
24. Tozzi V, Balestra P, Galgani S, Narciso P, Sampaolesi A, Antonio A, et al. Changes in neurocognitive performance in a cohort of patients treated with HAART for 3 years. J Acquir Immun Defic Syndr 2001;28:19-27.
25. Frank EG, Foley GM, Kuchuk A. Cognitive functioning in school-age children with human immunodeficiency virus. Percept Mot Skills 1997;85:267-72.
26. Jeremy RJ, Kim S, Nozyce M, Nachman S, McIntosh K, Peslosi S, et al. Pediatric AIDS Clinical Trials Group (PACTG) 338 and 377 Study Teams. Neuropsychological functioning
and viral load in stable antiretroviral therapy-experienced HIV-infected children. Pediatrics 2005;115:380-7.

28. Weber E, Woods SP, Cameron MV, Gibson SA, Grant I. HIV Neurobehavioral Research Center Group. Mental rotation of hands in HIV infection: Neuropsychological evidence of dysfunction in fronto-striato-parietal networks. J Neuropsychiatry Clin Neurosci 2010;22:115-22.

29. Hochhauser CJ, Gaur S, Marone R, Lewis M. The impact of environmental risk factors on HIV-associated cognitive decline in children. AIDS Care 2008;20:692-9.

30. Huston AC, Mcloyd VC, Coll CG. Children and poverty: Issues in contemporary research. Child Dev 1994;65:275-82.

31. Nozyce ML, Lee SS, Wiznia A, Nachman S, Mofenson LM, Smith ME, et al. A behavioral and cognitive profile of clinically stable HIV-infected children. Pediatrics 2006;117:763-70.

How to cite this article: Ravindran OS, Rani MP, Priya G. Cognitive deficits in HIV infected children. Indian J Psychol Med 2014;36:255-9.

Source of Support: Nil, Conflict of Interest: None.