HIV-related referrals to a local pediatric neuropsychology clinic: A 1-year demographic and neuropsychological profile

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SIGNATURE:

STUDENT NUMBER: DVDNAA001 and MKNLIM001
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-Naaila Davids

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-Limplo Mokoena
Abstract

Human immunodeficiency virus (HIV) is a serious public health concern, which is the leading cause of mortality in South Africa. Children are unduly affected and experience both direct and indirect effects associated with the disease, seen in a range of domains including medical, developmental, cognitive, psychosocial and academic spheres. The main aim of this study was to describe the demographic (including social, medical, developmental and academic) and neuropsychological profiles of children referred to the Red Cross War Memorial Children’s hospital’s (RXH) pediatric neuropsychology clinic (PNC), over a one-year period for HIV-related neuropsychological difficulties. The study design was retrospective and both qualitative and quantitative, as a case series approach was adopted. A total of \( N=41 \) children were referred to and seen at the RXH PNC in 2015. The main focus of the current study was however on the subsample of children who were referred for HIV-related difficulties \( (n=20) \). The results indicated that the mean age of the subsample was, approximately 10 years. Most were male, isiXhosa-speaking, and from low socio-economic backgrounds. A number of children in the subsample had developmental delays, and language and behavioural difficulties. Additionally this subsample had academic difficulties as the majority (70%) had failed at least one grade. The results of the neuropsychological assessments showed that, on average, the children scored quite poorly across the domains of attention, executive functions (including working memory and abstraction), language, processing speed and general intellectual functioning. However, what was inconsistent with previous literature is that children performed in the average range for memory. Memory problems were reported for many children in the sample, however the neuropsychological reports suggest that these difficulties may be a function of attentional problems and not pure memory problems per se. Future research is important to substantiate this finding as it can begin to inform intervention strategies.
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Human immunodeficiency virus (HIV) is a serious public health concern, which was first reported in the 1980s and since then has been the leading cause of mortality in South Africa (Ortblad, Lozano, & Murray, 2013). Children are unduly affected and experience both direct and indirect effects associated with the disease, seen in a range of domains including medical, developmental, psychosocial and academic spheres. Among the direct effects, one of the primary areas of concern is that of the impact of HIV on neurocognitive development and outcomes. Since direct and indirect effects are interrelated, there are a number of domains that may be impacted by these neurocognitive effects (e.g., social and academic spheres) and a number of factors that can also impact neurocognitive outcomes. Despite the local impact, recent local epidemiological data are lacking. Such data are important in terms of designing and implementing interventions that are contextually relevant.

**Epidemiology**

According to UNAIDS (2013; 2015), in 2012 and 2014 the global estimates of people living with HIV were approximately 35.3 and 39.9 million, respectively. In 2014, approximately 2 million people were newly infected with HIV, including 200,000 children; and 1.2 million people died of Acquired Immunodeficiency Syndrome (AIDS) related illnesses globally (UNAIDS, 2013). In June 2015, 15.8 million people globally, had access to antiretroviral (ARV) therapy, increasing their chances of living a longer and healthier life (UNAIDS, 2015).

There are clear global disparities in the HIV epidemiology between high-income (HIC) and low- and middle-income countries (LAMICs) (Cock & Weiss, 2000). The countries with the highest prevalence rates in the world are LAMICs located in Sub-Saharan Africa (Connolly, Colvin, Shishana, & Stoker, 2004). In 2013, approximately 24.7 million people were living with HIV in Sub-Saharan Africa of which approximately 2.9 million were children (UNAIDS, 2013). Within this location, South Africa leads with the highest infection rate globally (Jemmott et al., 2014).

In 2013 there was an estimated 6.3 million people in South Africa living with HIV. In the same year, there were approximately 330,000 new infections with an additional 200,000 South
Africans who died from AIDS related illnesses which were caused by the HIV virus (UNAIDS, 2013). Additionally in the year 2015 there was an estimate of 7 million people living with HIV in South Africa, of which 240 000 were children aged 0-14 (UNAIDS, 2015).

In South Africa those living with HIV are predominantly females in their reproductive years. This is concerning for children, bearing in mind that a common route for HIV transmission is from mother to child during pregnancy (Jemmott et al., 2014; Puthanakit et al., 2013). There are three distinct ways in which a child can acquire HIV from the mother: during pregnancy, during delivery, or during breastfeeding (Puthanakit et al., 2013).

Despite the local impact of HIV and the available epidemiological data, more local and pediatric focused data are needed. HIV infection differs in its pathology in adults and children; therefore extrapolating results from adults to children is not feasible (Cohen et al., 2015).

**HIV Pathogenesis**

The onset of HIV is initially asymptomatic, but eventually leads to the progressive decline of the immune system resulting in susceptibility to opportunistic infections and diseases (Naif, 2013). Only at three months post-infection, when seroconversion occurs in which HIV-specific antibodies can be detected, does the individual start experiencing symptoms (Naif, 2013). During primary infection, although the body may appear to be healthy, the virus duplicates in the lymph nodes and the bloodstream of infected individuals. This may result in the slow damage of the immune system through the increase of viral load in the body (Naif, 2013).

The immune system plays a role in protecting the body by identifying antigens or attacking bacteria and viruses (Kumar & Herbein, 2014). The virus therefore weakens it as it infects a number of different immune cells, in particular macrophages and CD4+ T cells (Kumar & Herbein, 2014). There is constant communication between these cells, which facilitates the transmission of HIV (Kumar & Herbein, 2014). Typically, women who show positive results on p24 antigen tests and who have a low CD4 cell counts, show greater likelihood in the mother-to-child transmission of HIV (Lambert & Stiehm, 1993; WHO, 2015).

**HIV and the Central Nervous System**

Initially, at the outset of the HIV/AIDS epidemic, it was assumed that only the immune system was vulnerable to the effects of the virus (Byers, 2001). However, it is now clear that the
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The central nervous system (CNS) is particularly vulnerable to the impact of HIV too. The virus has an impact on subcortical and grey matter structures in the CNS, which leads to the clinical syndrome that has poor motor, behavioural and cognitive manifestations (Valcour, Sithinamsuwan, Letendre & Ances, 2011). Consequently, there is a range of resultant neuropsychological sequelae associated with HIV infection. These neuropsychological sequelae might be considered direct effects of CNS damage. Another example of a direct effect is the neurodevelopmental problems described in association with HIV. There is also a range of indirect effects of HIV, such as psychosocial and academic problems, which may be secondary to the neuropsychological and developmental problems (Smith et al., 2006).

**Neurodevelopmental and neuropsychological effects of HIV in children**

Many studies on the neurological and neuropsychological outcome of HIV infection focus on the effects on the adult brain; however this research cannot be applied to children, given the different routes and time course of infection across these developmental stages (Andronikou et al., 2014). With pediatric infections (e.g., in perinatally infected children), the effects may be worse as it not only impacts children and adolescents on their physical growth, but their psychological health and neurodevelopment too (Smith et al., 2006). Developmental delays and neurological complications are frequently seen in children with HIV, especially in children who were infected perinatally (Potterton et al., 2009).

Delays in mental and motor development are prominent from as young as 4 months of age, and continue into children’s pre-school years (Smith et al., 2006). Other than motor skills, neuropsychological impairment is frequently reported in the domains of general intellectual functioning, language, attention and executive functions, learning and memory, visual-spatial abilities and information processing speed (Cohen et al., 2015; Van Rie, Harrington, Dow, & Robertson, 2007). HIV-infected children also often exhibit behavioural impairments, such as impulsivity and hyperactivity, which, together with attentional deficits, have been linked to attention-deficit/hyperactivity disorder (Nozyce et al., 2006). Thus the potential effect of HIV on the CNS of children can be detrimental as it can affect their ongoing cognitive development. All of these sequelae can often then have knock-on effects in terms of academic outcomes (Puthanakit et al., 2010).
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**Academic effects**

Since the majority of HIV infected children are orphaned, they are more vulnerable to being enrolled in schools late. Higher levels of absenteeism and lack of school completion amongst these children is common due to the stigma attached to the illness and they may experience bullying (Chuong & Operario, 2012; Gilborn, 2002; Guo, Li, & Sherr, 2012). Additionally, children with HIV also tend to be delayed due to the neuropsychological effects of HIV and therefore perform more poorly than non-infected children (Walker et al., 2011). It is therefore imperative for early learning opportunities to be implemented as delays in this regard can lead to a loss of developmental potential (Walker et al., 2011).

**Treatment and psychosocial issues**

The purpose of antiretroviral therapy (ART) is to suppress the HIV from further progression (WHO, 2015). The combination of three ARV drugs, Efavirenz, Etravirine, and Nevirapine (nonnucleoside reverse transcriptase inhibitors, NNRTIs) is referred to Highly Active Antiretroviral Therapy (HAART). ARV adherence is key to suppressing the virus, however this can be quite complex in the South African context (Haberer & Mellins, 2009).

Despite access to ARVs in some countries (e.g., South Africa), HIV/AIDS still affects millions of children in LAMICs as a result of poor adherence. Socio-economic barriers, misclassification of the HIV stage, and insufficient awareness about the disease and its consequences all contribute to poor ARV access and adherence (Jemmott et al., 2014; Kimani-Murage, Manderson, Norris, & Kahn, 2013). A structural barrier (that prevents adherence to pediatric ART) is the high levels of poverty/unemployment of the caregivers of children with HIV, which creates difficulties in travelling far distances to health facilities for ART collection for example (Kimani-Murage et al., 2013). Additionally caregivers believe that local health workers might breech the confidentiality of their children’s HIV status and are therefore reluctant to present their child for care. Caregivers fear the social costs, such as stigma and discrimination, which are associated with disclosing the HIV status of their child (Kimani-Murage et al., 2013). However, despite room for improvement, in Sub-Saharan Africa, the implementation of ART has resulted in a decline in the mortality rates of children living with
HIV, quickly changing the status of HIV from fatal to a chronic disease (Coovadia et al., 2015). This outcome, however, relies on the timing of ARV initiation.

A delay in ARV initiation slows down immunologic reconstitution and therefore timing of the ART is critical for optimizing neurodevelopment and cognitive performance (Donald et al., 2012). The administration of ART typically before 1 year of age is associated with a significantly better neurodevelopmental outcome in children (Violari et al., 2008). With that, the presence of an AIDS-defining condition before ART initiation is associated with lower cognitive scores in perinatally-infected children and adolescents (De Baets, Bulterys, Abrams, Kankassa, & Pazvakavambwa, 2007; Donald et al., 2012). Not only do ARVs promote normal growth, but prolong the survival rate, and have been known to improve the quality of life (Smith et al., 2006).

In sum, HIV remains a serious public health problem in South Africa. There is a range of associated neuropsychological, behavioural, academic, and emotional problems that may ensue. In order to understand the needs of the child infected with HIV, one needs to understand the child in the context of all of these domains. Although treatment in the form of ARVs is now more readily available, there are psychosocial issues that impact access and adherence. Although broader epidemiological data is available, more local, site-specific profiling is needed for interventions that may target children being treated at these sites.

Aims and hypotheses

The aim of this study is threefold. First, we aim to establish the proportion of children referred to the Red Cross War Memorial Children’s hospital’s (RXH) pediatric neuropsychology clinic (PNC), over a one-year period for HIV-related neuropsychological difficulties relative to the total number of children referred to the PNC for various neuropsychological problems related to neurological- or neurosurgical-related diagnoses (including HIV). Second, we aim to describe the demographic (including social, medical, developmental and academic) profile of these children diagnosed with HIV and referred to the PNC over a one-year period based on the neuropsychological reports provided by the PNC for these children. Third, we aim to describe the neuropsychological profile of the same children over the same time period, also based on the neuropsychological reports. For both these two latter aims, our objective is to identify and report
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on common trends in the reports of these children with the hope of identifying areas for possible intervention. Given that the proposed study is exploratory, there are no stated hypotheses.

Methods

Design and setting

The current study involved the description and analysis of neuropsychological case reports of children admitted to the RXH’s PNC over a one-year period (i.e., 2015). The study design was retrospective and both qualitative and quantitative, as a case series approach was adopted. The results included both qualitative (thematic) analyses of the data and descriptive statistics of the neuropsychological case reports. Combining these research methods is increasingly being used with the prospect of a multifaceted observation based on the subject matter (Foss & Ellefsen, 2002).

The data was stored at RXH; hence this was the primary study site.

Participants

Participants for this study included the children whose neuropsychological reports were reported on in this study, i.e., children referred to the PNC at RXH in 2015. We mainly focused on a subsample of these children, i.e., the children referred for HIV-related difficulties (i.e., all children who were referred to the PNC who were HIV positive who were referred for direct (e.g., neurocognitive) or indirect (e.g., consequent academic problems) effects, specifically related to their HIV status). The participants included boys and girls, 12 years and under, as the RXH usually only admits children up to 12 years of age. We included all children admitted to the clinic for 2015 in terms of our first aim. For aims two and three, we only focused on children referred to the clinic for HIV-related neuropsychological and/or related difficulties.

Measures

The neuropsychological measures reported on in the results of the current study are those that were listed in the neuropsychological reports of the PNC. These included a variety of subtests from standardized neuropsychological batteries, commonly used at the PNC. These tests

1 The RXH usually only admits children up to 12 years of age. Some children are however still followed up after the age of 12. Therefore, we had one child in our sample who was 13 years of age.
formed the basis of the neuropsychological outcomes described. For a full review of all measures that were included in the case reports, please refer to Appendix A.

**Procedure**

Once ethical approval for the study was obtained, we gained access to the neuropsychological reports for the PNC for 2015 via the clinic coordinator. We then accessed the files at RXH and then tallied up the number of referrals for HIV-related difficulties vs. other and separated the reports into these two batches. We each looked at all of the case records for HIV-related referrals and scanned the reports for meaningful trends in the referral notes, as well as in the medical, developmental, social, and academic histories for each child. We then compared and collated our findings. Regarding the information about the children’s medical, developmental, social, and academic history reported, this was gleaned from the history sections of the neuropsychology reports from the PNC. That information in the reports was based on information from the children’s medical folder and from information obtained during the history taking sessions with parents/guardians done at the PNC. We also looked at trends in the parent and/or teacher concerns, which were noted, the neuropsychological test performances, and at the conclusions and recommendations for each child. We then recorded the tests used and the outcome scores for the neuropsychological tests for each child for analysis.

**Data Analysis**

**Case series.** The case series as a research strategy is useful for understanding the complexity associated with social phenomena as this method propagates for holistic insight within specific research areas. It therefore forms an essential part of social science inquiry (Kohlbacher, 2006; Yin, 2011). The case series as a research strategy is not bound to one research method; rather it comprises an all-encompassing method meaning, qualitative, quantitative or both research methods may be used (Kohlbacher, 2006). This type of inquiry is said to be a heterogeneous activity because it includes a broad scope of coverage, from single case studies up to multiple cases and includes varied levels of analysis, from individual to groups, all the way to organizational fields (Kohlbacher, 2006; Yin, 2011). There are three main steps in undertaking case series:
Step 1. Collecting evidence. According to Kohlbacher (2006) there are multiple avenues to seek for evidence for case series which could include: archival records, observations (direct or participant), interviews or physical artifacts. Using these different avenues can be beneficial if: 1) if multiple sources are used for evidence, 2) creating a database for the case study and 3) maintaining a series of this evidence (Yin, 2011). We collected our evidence by the use of archival records obtained from RXH.

Step 2. Analyzing case study evidence. This step involves a thorough explanation of the data with detailed reference to the categories or themes that have been deemed important during the process of analysis (Kohlbacher, 2006). In this step the data can be structured according to themes that enhance the purpose of the research. Lastly, the data then needs to be scrutinized to see how well (or not) they fit the expected categories (Kohlbacher, 2006). In this step we searched through meaningful information needed for analyzing the data under each of the case report sections: reason for referral, medical, developmental, social and academic history, parent and/or teacher concerns at the time of the assessment, the neuropsychological test scores, and the impression and conclusion sections. We were guided by the literature in terms of identifying important information that was relevant to the child with HIV under these headings. We then generated key themes for all pieces of relevant information that we identified in the case reports to determine the most appropriate themes and how these align with the research question and lastly searched for common trends extracted from the case reports.

Step 3. Reporting case series. In this final step, the results and the findings of the case series needs to be concluded and reported (Kohlbacher, 2006). As a final step in our data analysis we documented the findings of the cases reviewed.

Descriptive analyses. For this component, we used SPSS version 23 to analyze the data. We present descriptive statistics for a range of variables: the demographic profiles (i.e. age, language and sex), social profiles (i.e. number of people in a household, where they resided, parents’ education and employment, and whether the parents were alive or not), medical profiles (i.e. developmental milestones, behavioural problems, attentional problems, language-related difficulties, ear infections or hearing problems, age of diagnosis and ARV initiation), developmental profile (i.e. whether they were delivered prematurely or not, whether the mother
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consumed alcohol / smoked (or not) during the pregnancy), and school history (i.e. current grade, whether they failed a grade or not). We then presented a descriptive analysis of the neuropsychological test scores and reported on how these samples of children were performing across domains.

Ethical considerations

Ethical approval was obtained from the Department of Psychology’s Research Ethics Committee (see Appendix B) and the Faculty of Health Sciences Human Research Ethics Committee (see Appendix C). We also obtained permission to use the neuropsychological records at RXH from the hospital administrators (see Appendix D). In terms of informed consent, parents / caregivers of children assessed at the PNC are routinely asked for their consent that their data be used for research purposes. Hence, we only included data where parents provided such consent (see Appendix E for consent form used at the PNC). Other ethical considerations include confidentiality, which includes the non-disclosure of the case report information, as well as anonymity, which entails not including the patients’ names or any explicit identifiers in our analyses or write-up.

Results

Demographics of the overall sample of referrals to the PNC for 2015

In terms of the overall sample \((N = 41)\), which includes all the children that were referred to the pediatric neuropsychology clinic (PNC) at the RXH in the year 2015, the average age in months was \(M = 121.58\) (\(SD = 34.48\), approximately 10 years), with a range of 55 – 197 months. Four different languages were spoken amongst the participants, including isiXhosa \((n = 21; 51.2\%)\), English \((n = 15; 36.6\%)\), Afrikaans \((n = 4; 9.8\%)\) and Sesotho \((n = 1; 2.4\%)\). Within the sample, 73.2% of the children that were referred to the PNC at RXH were male.

In terms of the frequency of neuropsychology assessments, 25% of the sample had returned to the RXH PNC for a reassessment while 75% were being assessed for their first time. There were a wide variety of reasons pertaining to why the children had been referred to PNC. These included neuropsychological difficulties related to epilepsy, behavioural difficulties (including ADHD), general developmental delays, academic concerns and school placement and
assessments of overall cognitive functioning and neuropsychological difficulties related to HIV. Approximately half of the referrals \((n = 20; 48.8\%)\) to the PNC for 2015 were specifically HIV-related.

**Demographics of subsample of children referred to the PNC for HIV-related difficulties specifically**

With reference to the children diagnosed with HIV, the average age in months was \(M = 122.85\) \((SD = 34.48, \text{approximately } 10 \text{ years})\), with a range of 76 – 158 months. Three different languages were spoken amongst the participants, including isiXhosa \((n = 15; 75\%)\), English \((n = 4; 20\%)\) and Afrikaans \((n = 1; 5\%)\). Information regarding race was not available for participants, even though it may be assumed that those who were isiXhosa-speaking may be of the Black African race. In personal communication with one of the PNC clinicians, there were no non-Black African children seen at the clinic in 2015 who were isiXhosa-speaking (Personal communication with Dr Leigh Schrieff-Elson, 10 November 2016). Further, the race of those who were English or Afrikaans-speaking cannot be assumed. Within the subsample, 55% of the children were male.

The results below all pertain specifically to this subsample of children. Almost half \((45\%; n = 9\) of history-taking sessions with the families of these participants were conducted with the mothers. In other cases the child's history was provided by grandparents, aunts or foster parents, and where this information was available, by social workers. Hence, in some of the cases there is missing data in terms of the medical history for children for whom information could not be obtained (e.g., children in foster homes where the child's full history is unknown).

**Social history**

Regarding the social history of the participants referred to the PNC for HIV-related difficulties, the number of people who lived with the participants (information which was known for 90% \((18/20)\) of the subsample) ranged from 2-9 people per household, with a mean of 4 per household. In most cases the specific areas in which these families live were unknown; however it can be assumed that most, if not all reside in the Western Cape since none were noted to be from out of town. The reports that do provide the area in which the families resided \((n = 6)\)
include places such as Wallacedene Crossroads, Heinz Park, Gugulethu, Blackheath, Bonteheuwel and Philippi.

With reference to the educational history of the parents, this information was reported in 6 out of the 20 cases (30%). In some cases information was available for both parents but not for others. Hence, of the 6 sets of parents, educational background was reported for 9 individual parents, while information was missing for the other 3. Among the 9 parents, one parent had not received a secondary education. Of the remainder of the parents who had received secondary schooling, 37.5% (n = 3) had matriculated but the rest (50%; n = 5) did not complete their secondary schooling. For the rest of the subsample’s parents, 2 were reported as being uneducated while the rest of the information is unknown (for 26 out of the 40 parents).

For the parents who indicated that they were employed (6 individual parents), their current occupations included petrol attendant, caregiving, domestic worker, courier driver, security guard and self-employment. Unemployment was noted for 3 additional parents (both mothers and fathers). The rest of the information regarding current or previous employment was unknown for 42.5% (17/40) of mothers and fathers due to parents currently not being present in the children’s lives.

Within the subsample (n = 20), 50% (n = 10) of the children have both or at least one deceased parent, of which 80% (n = 8) had a mother who was deceased, 10% (n=1) had a father who was deceased and 10% (n = 1) had both parents deceased. In some cases, there was no information regarding the parents (15%; n = 3), this was in cases that involved foster or orphaned children.

**Medical History**

The medical history of the participants referred to the PNC for HIV-related difficulties, that is, medical issues over and above the positive diagnoses of HIV and treatment related information (which is discussed below), is shown in Table 1. Table 1 shows that within the sample only 1 (5%) participant included a formal diagnosis of ADHD. In terms of developmental delays, this was reported for 80% of the children with HIV, which accounts for more than half of the children within that group not reaching some or all of their age-appropriate developmental milestones. With regards to language-related problems, a range of difficulties were reported for
11 (55%) participants. These included poor verbal skills with a lack of extensive vocabulary for their age and difficulties concerning reading, writing, spelling and comprehension. In terms of behavioural problems (40%), these problems included anger, defiance and aggressive behaviour. Ear infections and/or related hearing problems were reported for about 75% of participants. Some of the ear infections that were reported included chronic suppurative otitis media (persistent inflammation of the middle ear) and auricular (external ear canal) abscesses. In other children hearing problems were reported where some needed hearing aids or needed to focus intensely in order to hear what was being communicated to them.

Table 1
Problems noted in the medical history of children referred to the PNC at RXH for HIV-related difficulties (other than HIV diagnosis and treatment-related issues)

<table>
<thead>
<tr>
<th></th>
<th>Suspected</th>
<th>Diagnosed/reported</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>6 (30%)</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Developmental delays</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Language difficulties</td>
<td></td>
<td>16 (80%)</td>
<td></td>
</tr>
<tr>
<td>Behavioural difficulties</td>
<td></td>
<td>11 (55%)</td>
<td></td>
</tr>
<tr>
<td>Hx of ear infections</td>
<td></td>
<td>8 (40%)</td>
<td></td>
</tr>
<tr>
<td>Hx of hearing problems</td>
<td></td>
<td>9 (45%)</td>
<td></td>
</tr>
</tbody>
</table>

Note. The abbreviation Hx refers to the history of the ear infection or hearing problems.

**Age at HIV diagnosis and antiretroviral initiation.** Out of the 20 participants who were diagnosed with HIV, the age of diagnosis was reported for 16 participants. For those participants, the mean age of diagnosis in months was $M = 18.83$ months ($SD = 36.92$, range: 1 week – 144 months (12 years)). Additional information about the mother’s HIV status was reported in 10 cases in which 9 mothers reported that they were positive and 1 was negative. The rest of the information was unknown.

The average age of ARV initiation was $M = 30.15$ months ($SD = 37.66$, range: 4 months – 12 years). Whether patients were compliant or not was reported in 16 out of the 20 cases. Out of the 16 cases, 11 were compliant while 4 were not. Some of the reasons for non-compliance included social issues such as missed appointments to receive ARV treatment or separation from
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parents. Other reasons involved parents/guardians who were forgetful or children who were oppositional to taking the medication.

Table 2 shows the frequencies of 1) how many children were diagnosed with HIV, and 2) how many children were started on ARVs, before they were a year old, between 1 and 2 years old and 2 years and older. Figures 1 and 3 are graphical representations of the descriptive statistics pertaining to the age of HIV diagnosis and age at ARV initiation, respectively. Figures 2 and 4 show the same information for each of the participants in the subsample, respectively. The reference line across Figure 2 indicates that most of the children were diagnosed with HIV before 18 months. Additionally, the reference line in Figure 4 indicates that 12 out of 20 children initiated ARVs after 12 months.

Table 2
Frequency table showing the ages at which children were diagnosed with HIV and ARVs were initiated

<table>
<thead>
<tr>
<th></th>
<th>Less than 1 year</th>
<th>Between 1 and 2 years</th>
<th>Older than 2 years</th>
<th>Missing data</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV diagnosis</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>ARV initiation</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>0</td>
<td>20</td>
</tr>
</tbody>
</table>

Note. The range of the children who initiated their ARVs after 24 months (2 years) is 13-144 months. The abbreviation HIV stands for Human immunodeficiency virus and ARV stands for Antiretrovirals.
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Figure 1. Boxplot indicating descriptive statistics for age of HIV diagnosis.

Figure 2. Age at diagnosis for individual participants
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Box plot indicating age at ARV initiation in months

Figure 3. Boxplot indicating descriptive statistics for age of ARV initiation.

Bar graph indicating individual cases and their age at ARV initiation in months

Figure 4. Age at ARV initiation for individual participants.
Developmental history

Regarding the developmental history reported by family members/caregivers, or gleaned from the hospital files, the gestation period was reported in 9 of the 20 cases with the average gestation period of $M = 8.55$ months ($SD = 0.88$; range: 7 – 10 months, in which 4 children were delivered earlier than 9 months). Of the 4 children, 1 child was delivered at 7 months and the other 3 at 8 months. Regarding the rest of the children 5 were carried to term, leaving unknown data for 11 cases of the sample. The majority of the mothers of the children (55%; $n = 11$) had a normal vaginal delivery, while 15% ($n = 3$) of the mothers had a caesarean and the rest were unknown (30%; $n = 6$). The average birth weight for the 10 cases in which birth weight was reported was $M = 2.90$ kg ($SD = 0.61$, Range: 2.20-4.0 kg).

Table 3 indicates that there were a various problems that were reported during the gestation period. Issues such as illness or complications during the pregnancy were reported for (25%; $n = 5$) of the sample. Table 3 also includes information about whether mothers consumed alcohol or smoked during their pregnancy.

Table 3

| Smoking, alcohol consumption and other problems noted during the gestation period |
|---------------------------------|---------|---------|---------|---------|---------------------------------|
|                                  | Yes     | No      | Unknown | Total   |
| Description of problems          | $n$ (%)  | $n$ (%)  | $n$ (%)  | $n$     |
| Problems during pregnancy        | 5 (25%)  | 9 (45%)  | 6 (30%)  | 20      | Some of the problems during pregnancy included the mother being ill, complications during pregnancy and the neglect of prenatal care. |
| Alcohol consumption              | 6 (30%)  | 9 (45%)  | 5 (25%)  | 20      |
| Smoking                          | 2 (10%)  | 12 (60%) | 6 (30%)  | 20      |

Note. Out of the 6 cases in which alcohol consumption was reported, majority of the mothers drank heavily or almost every day. Additionally some 1 child was reported to have FAS and one other was suspected to have FASD.
Additionally it was reported that among the 11 children (55%) for whom this information was reported, 6 of the known cases were breastfed and 5 were not breastfed while the rest were of cases were unknown (45%; \( n = 9 \)). Cases of early separation between mother and child were reported in 6 of the 20 cases (30%) and descriptions of these separations include the death of the mother, neglect, abandonment and living in foster homes.

**Developmental Milestones.** The language and gross motor milestones for the children with HIV are presented in Table 4. This table clearly indicates the delayed development of language and motor milestones.

Table 4
Developmental milestones comparing the appropriate mean age to the mean age of the participants diagnosed with HIV

<table>
<thead>
<tr>
<th></th>
<th>n (reported milestones)</th>
<th>Appropriate mean age for milestones* (months)</th>
<th>Mean (months)</th>
<th>SD</th>
<th>Min (months)</th>
<th>Max (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First words</td>
<td>13</td>
<td>9</td>
<td>16.92</td>
<td>8.25</td>
<td>7</td>
<td>36</td>
</tr>
<tr>
<td>Two words</td>
<td>8</td>
<td>18</td>
<td>26.63</td>
<td>6.30</td>
<td>18</td>
<td>36</td>
</tr>
<tr>
<td>Talking in sentences</td>
<td>8</td>
<td>24</td>
<td>48.13</td>
<td>8.34</td>
<td>36</td>
<td>60</td>
</tr>
<tr>
<td>Sitting</td>
<td>13</td>
<td>8</td>
<td>9.15</td>
<td>4.59</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Crawling</td>
<td>9</td>
<td>9</td>
<td>12.88</td>
<td>5.75</td>
<td>7</td>
<td>24</td>
</tr>
<tr>
<td>Walking</td>
<td>16</td>
<td>14</td>
<td>22.43</td>
<td>10.28</td>
<td>9</td>
<td>48</td>
</tr>
<tr>
<td>Tying shoelaces</td>
<td>6</td>
<td>48</td>
<td>72.00</td>
<td>16.97</td>
<td>48</td>
<td>96</td>
</tr>
<tr>
<td>Buttoning clothing</td>
<td>10</td>
<td>60</td>
<td>76.8</td>
<td>22.05</td>
<td>48</td>
<td>120</td>
</tr>
<tr>
<td>Dressing</td>
<td>10</td>
<td>48</td>
<td>70.8</td>
<td>24.94</td>
<td>36</td>
<td>120</td>
</tr>
<tr>
<td>Writing</td>
<td>9</td>
<td>60</td>
<td>74.66</td>
<td>23.06</td>
<td>36</td>
<td>120</td>
</tr>
</tbody>
</table>

*Note. SD= Standard Deviation of the mean. Min and Max represent the minimum and maximum ages (in months) respectively, at which milestones were reached. *The appropriate mean ages for milestones according to Peterson (2013).*

**School history**

In terms of the school history of the participants referred to the PNC for HIV-related difficulties, 50% \( (n = 10) \) of the children had previously attended grade R, and out of these 10
children 1 child had to repeat grade R. As for the other 50%, they either did not attend grade R, 
\( n = 3 \) because they were too old or information regarding Grade R attendance was not provided 
\( n = 7 \). Additionally, 14 out of the 20 children (70%) failed at least one grade or did not 
complete a grade. Out of the 14 children, the majority failed grade 1 \( n = 8; \) 57.14\%. The 
common grades that were failed besides grade 1 were grade 4 \( n = 5, \) 35.71\%, grade 2 and 3 \( n 
= 4, \) 28.57\%. In the year 2015, the grades that participants were attending at the time of their 
assessments ranged from grade R to grade 5.

In terms of collateral information provided by the schools (in response to requests from 
staff and postgraduate students at the PNC), only 50\% of the reports provided collateral 
information. The common trends that were found within these reports included that most of the 
children seemed to have language and comprehension difficulties, specifically with spelling, 
reading, switching letters, difficulties with word formation and being slow in completing tasks. 
In contrast it seemed that some seem to have been better at oral assessments than those that were 
written.

**Neuropsychological assessments**

Table 5 provides a summary of the outcomes of the neuropsychological assessments the 
children underwent at the PNC at RXH. Not all participants were assessed on each subtest 
therefore this can account for the missing data or varying numbers of participants for each 
subtest reported in Table 5.

Table 5 shows that the participants scored quite poorly across the domains of attention, 
executive functions (including working memory and abstraction), language, processing speed 
and general intellectual functioning. The qualitative descriptions of their scores largely range 
from extremely low, to low average. In contrast, in the memory and planning domains, the 
participants performed relatively well with qualitative descriptions of their scores being mainly 
average.
HIV-related referrals to a local pediatric neuropsychology clinic: A 1-year demographic and neuropsychological profile

Table 5
Results of the neuropsychological assessments the participants underwent, testing different cognitive domains

<table>
<thead>
<tr>
<th>Cognitive domain</th>
<th>Subdomain</th>
<th>Test</th>
<th>n</th>
<th>Qualitative score</th>
<th>M (standardized score)</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>Sustained attention/concentration</td>
<td>CMS: Numbers forward</td>
<td>20</td>
<td>Borderline</td>
<td>5.75</td>
<td>2.88</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Selective attention</td>
<td>TEA-Ch: Sky Search</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Targets</td>
<td>7</td>
<td>Low Average</td>
<td>6.57</td>
<td>4.39</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time per target</td>
<td>7</td>
<td>Extremely Low</td>
<td>3.29</td>
<td>3.30</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attention score</td>
<td>5</td>
<td>Low Average</td>
<td>6.20</td>
<td>4.32</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Language</td>
<td></td>
<td>NEPSY: Comprehension of Instructions</td>
<td>9</td>
<td>Borderline</td>
<td>4.56</td>
<td>2.01</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Memory</td>
<td>Verbal memory</td>
<td>WRAML: Verbal Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Learning</td>
<td>19</td>
<td>Average</td>
<td>8.73</td>
<td>2.10</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delayed memory</td>
<td>19</td>
<td>Average</td>
<td>8.05</td>
<td>2.66</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recognition</td>
<td>19</td>
<td>Low Average</td>
<td>6.42</td>
<td>2.89</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NEPSY: Word List</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediate recall</td>
<td>1</td>
<td>Average</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delayed</td>
<td>1</td>
<td>Average</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
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<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>Recognition</td>
<td>1</td>
<td>Average</td>
<td>9</td>
<td></td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Visual memory</td>
<td>CMS: Dot Locations</td>
<td>Learning</td>
<td>10</td>
<td>Average</td>
<td>8.30</td>
<td>2.41</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immediate recall</td>
<td>12</td>
<td>Average</td>
<td>9.92</td>
<td>2.99</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delayed recall</td>
<td>12</td>
<td>Average</td>
<td>9.42</td>
<td>2.91</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Fine Motor Skills</td>
<td></td>
<td>NEPSY: Fingertip Tapping</td>
<td>5</td>
<td>Borderline</td>
<td>4.20</td>
<td>3.19</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Repetitions</td>
<td>5</td>
<td>Borderline</td>
<td>4.20</td>
<td>3.19</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sequencing</td>
<td>5</td>
<td>Extremely Low</td>
<td>3.80</td>
<td>3.11</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Processing Speed</td>
<td></td>
<td>WISC: Coding</td>
<td>17</td>
<td>Low Average</td>
<td>5.11</td>
<td>1.76</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Executive Functions</td>
<td>Planning and inhibition</td>
<td>DKEFS: Tower</td>
<td>Total achievement score</td>
<td>8</td>
<td>Average</td>
<td>8.50</td>
<td>2.51</td>
<td>5</td>
</tr>
</tbody>
</table>
HIV-related referrals to a local pediatric neuropsychology clinic: A 1-year demographic and neuropsychological profile

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<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Move accuracy ratio</td>
<td></td>
<td>8</td>
<td>Average</td>
<td>7.88</td>
<td>2.10</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Rule violation</td>
<td></td>
<td>7</td>
<td>Average</td>
<td>8.71</td>
<td>3.59</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Time per move ratio</td>
<td></td>
<td>8</td>
<td>Average</td>
<td>8.38</td>
<td>3.74</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Working memory</td>
<td>CMS: Numbers backwards</td>
<td>15</td>
<td></td>
<td>Low</td>
<td>6.40</td>
<td>2.74</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>WASI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td>FSIQ</td>
<td>15</td>
<td></td>
<td>Extremely Low</td>
<td>68.47*</td>
<td>12.39</td>
<td>44</td>
<td>90</td>
</tr>
<tr>
<td>Intellectual</td>
<td>PIQ</td>
<td>15</td>
<td></td>
<td>Borderline</td>
<td>76.13*</td>
<td>11.78</td>
<td>62</td>
<td>97</td>
</tr>
<tr>
<td>functioning</td>
<td>VIQ</td>
<td>15</td>
<td></td>
<td>Extremely Low</td>
<td>66.40*</td>
<td>11.69</td>
<td>45</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>Block Design</td>
<td>15</td>
<td></td>
<td>Borderline</td>
<td>5.33</td>
<td>1.59</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Matrix Reasoning</td>
<td>15</td>
<td></td>
<td>Borderline</td>
<td>4.67</td>
<td>3.64</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Vocabulary</td>
<td>15</td>
<td></td>
<td>Extremely Low</td>
<td>2.67</td>
<td>2.16</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Similarities</td>
<td>13</td>
<td></td>
<td>Borderline</td>
<td>4.38</td>
<td>2.63</td>
<td>1</td>
<td>9</td>
</tr>
</tbody>
</table>

*Note. Scores with asterisk (*) indicate T-scores while the rest of the scores are scaled scores. FSIQ means Full Scale IQ, PIQ means Performance IQ and VIQ means Verbal IQ. Descriptions of tests are available in Appendix A.

In Appendix F there are boxplots (Figure 5 to Figure 30) that visually depict the descriptive statistics for each of the subtests in table 5. Additionally there are bar graphs, found in Appendix G, (Figure 31 to Figure 46) to graphically represent the individual scores of the
participants for each subtest within the domains being tested. While the boxplots were done for each test the bar graphs were only done when \( n \geq 10 \).

**Impressions and recommendations made in the neuropsychology reports**

Within the sample of children who were referred to the PNC for HIV-related difficulties, 55% (\( n = 11 \)) of the participants were reported to have memory problems (by the parents or guardians). However, the neuropsychological results generally did not reflect difficulties in either the visuospatial or audioverbal memory domains. In specific cases where performances were problematic in either of these memory subdomains, clinicians at the PNC attributed these difficulties to attentional problems rather than memory problems per se, that is, children did not pay attention to the word lists that were read in the audioverbal memory task or to the dot stimuli in the visuospatial memory test, hence they could not remember it. Attentional problems (sustained and sometimes also selective attention problems) were reported in the PNC reports for 17 children out of the 20 children in the subsample of HIV positive children. The remainder of the participants did have minor attentional problems such as the inability to attend to complex information (such as attentional control or tests requiring inhibition), or their levels of attention would fluctuate.

Among the recommendations at the end of the reports for the children to enhance their quality of life, one common suggestion was for the children to be placed in special needs schools. Within the sample, this recommendation for special needs schooling was made for 75% (15/20) of the sample. Another recommendation put forward for children in the sample (in terms of the neuropsychology reports) was for interventions for verbal skills. This included ideas around assisting the children with opportunities for building their vocabularies and enhancing their reading, writing and comprehension skills. Further recommendations, for attention-related problems, included having the children work in distraction free environments (for example the absence of T.V and radio while the child does their homework), that children take regular breaks during their school days and have shorter teaching periods. Additionally there was a recommendation for the participants to work at a slower pace so as not lose focus. These suggestions for verbal language- and attention-related interventions were often made in conjunction with special needs schooling. One of the last recommendations made at the end of
the neuropsychological reports was that reward-based systems and positive reinforcement generally should be used to encourage the children to perform certain tasks as they may give up when tasks become too challenging.

Discussion

The aim of this research project was threefold. First, our aim was to conduct a case review to determine the proportion of children referred to RXH PNC for HIV-related neuropsychological difficulties compared to children referred for neuropsychological problems related to other neurological- or neurosurgical-related diagnoses over a one-year period. Our second and third aims were to describe the demographic (including social, medical, developmental and academic) and neuropsychological profiles of this subsample of children diagnosed with HIV, respectively, and to find common trends among these children in the hope of identifying areas for possible intervention. We discuss each of these aims and the relevant findings, below.

Aim 1: Proportion of children referred to and assessed at RXH’s PNC for HIV-related neuropsychological difficulties

The results show that 50% of the children referred to the PNC at RXH in 2015 had HIV-related difficulties. This outcome is not surprising in the South African context given that South Africa leads the highest infection rate globally with approximately 2.9 million children infected with HIV in sub-Saharan African reported in 2013 (Jemmott et al., 2014; UNAIDS, 2013), despite the decline in new infections among children between 2000 and 2015. The newly infected HIV rate remains exceedingly high in the highest-burden countries such South Africa (UNAIDS 2015).

Aim 2: Demographic, social, medical, developmental and academic profiles of HIV subsample

Demographic profile. In terms of demographics, children were on average, 10 years of age although their ages ranged from 6-13 years. Regarding age, the upper age range reflects the age of the children being admitted to RXH.
Although we do not have specific information about race, the large proportion of isiXhosa-speaking children in the subsample suggests a high proportion of Black African children. This result may be a function of many factors, for example, the demographics of the children admitted to the hospital generally. However, the result also aligns with literature, for example, the 2012 national survey conducted by the metropolitan municipality in South Africa reported black Africans as having the highest HIV prevalence compared to other racial groups (Shisana et al., 2015). Regarding most of the sample being male does not seem to be significant as far as the literature goes. For example the results of the 2012 national survey of South Africa that found no significant difference in HIV prevalence between males and females between ages 5 and 14 years of age (Shisana et al., 2015).

**Social history.** There were no formal measures of socio-economic status in the neuropsychological reports. However, the reports included data on the number of people in a home and the areas of residence for some children. In terms of the information we had for some of the children, there was an average of four people living in the homes but the range extended to 9 in 1 case. Where the areas of residence were reported, these were generally areas classified as poor, socio economically (Shisana et al., 2015). These findings are in line with the fact that most children seen at the RXH come “from exceptionally poor and marginalized communities” (http://childrenshospitaltrust.org.za/red-cross-war-memorial-childrens-hospital-2/).

Regarding the parents’ education, no parent had tertiary level education and few had completed grade 12. Some parents were unemployed and others had employment of an unskilled or semi-skilled nature. Again, these findings fit the demographic of the majority of the children and consequently their families, seen at the RXH.

Where this information was reported, half of children in the subsample had both or at least one parent deceased. Given the likelihood that the children in the sample were infected through vertical transmission it may be that the mothers could have died from HIV-related complications. This is in line with Bryant and Beard (2016) who reported that approximately 15.1 million children in sub-Saharan Africa have at least lost one or both parents due to HIV-related complications.
In sum, the social profile of the children in the sample fit an inverse relationship between level of income, education and employment status and HIV risk according to the (No, 2002). This is particularly true in the case of income, where relatively poor members of society are prone to HIV infection because of their low socio-economic status, lack of education as well as being specifically vulnerable to the dangers of everyday life as a result of their household situations when the majority of the families are from urban informal areas (No, 2002; Shisana et al., 2015).

**Medical History.** Developmental delays, in terms of children reaching their age-appropriate milestones as compared to a typically developing population of children, were common (80%) among the children in the sample. Potterton et al. (2009) assert that developmental delays are not an unusual occurrence amongst children with HIV. They explain that many children with HIV come from low socioeconomic backgrounds and that poverty and low parental educational levels exacerbate the negative outcomes associated with a child’s developmental progress (Lima et al., 2004 as cited in Potterton et al., 2009).

Further, in terms of behavioural problems, some children were suspected of having ADHD with only one child out of the sample having been formally diagnosed with ADHD. Despite this, following assessments, the majority of children in the sample were reported to have attentional problems in the outcomes section of the neuropsychological reports. Attentional problems (often with a hyperactivity component) are rife in HIV-positive children (Zeegers et al., 2010).

Etiologic factors regarding attentional problems associated with HIV infection are multifaceted and could include the outcomes of the infection (including the viral replication and the impact that has on the development of the brain), chronic inflammation, the toxicity of antiretroviral drug and social factors (Hazra, Siberry, & Mofenson, 2010). According to Gadow et al. (2010) ADHD is not readily diagnosed in children with HIV. In their study, only 12% of their sample (n= 319) had a formal diagnosis of ADHD. This low rate of diagnosis was accounted for by overlapping symptoms or stringent diagnostic criteria, which may be extrapolated to the current study.
Other behavioural problems found within the sample that is consistent with other research include the children being impulsive, aggressive or displaying deviant behavioural and emotional difficulties (Nozyce et al., 2006; Puthanakit et al., 2010). Various language-related difficulties were reported in majority of the cases in the sample. Tomblin, Oleson, Ambrose, Walker and Moeller (2014) make an interesting connection between the effects of hearing loss and language development amongst children with HIV, and the negative implications of children losing their hearing during their window period of language development. In addition to language-related problems, ear infections or hearing problems were also reported for the sample in the current study. Chao et al. (2012) describe that ear infections are frequent amongst children with HIV and there is a high chance of these infections being a risk factor for hearing loss, which one may conjecture, could consequently affect language development.

Mode of transmission, age at HIV diagnosis and antiretroviral initiation. Although mother-to-child transmission could have been one possible means through which children contracted HIV (except in the case where the mother explicitly stated that she was HIV negative), we did not have access to information on the exact mode of transmission of HIV in the sample. However, Puthanakit et al. (2013) explains that one of the common ways of HIV transmission is through delivery (i.e., mother-to-child transmission). Additionally breastfeeding is another way in which HIV can be transmitted (Puthanakit et al., 2013). Within the sample only 10 mothers had reported their HIV status in which 9 were positive and 1 was negative. For those children for whom this information was included (70%), most (78.57%) were delivered through normal vaginal delivery. Additionally for the information given in terms of breastfeeding (55%), most (55%) were breastfed.

Out of the 20 participants who were diagnosed with HIV, the age of diagnosis was reported for 16 participants, with the average age of diagnosis being approximately 1 year and 6 months. The average age of antiretroviral (ARV) initiation was approximately 2 years and 6 months. Although most children were diagnosed and had ARVs initiated at a young age, box plots for these results show that 8 children were diagnosed and initiated ARVs after age 1. The consequences of delayed ARV initiation include the slowing down of immunologic reconstitution, affecting children’s neurodevelopment and cognitive performance (particularly
evident in their academic performance discussed below) (Donald et al., 2012). Hence the administration of ARV before 1 year is associated with significantly better neurodevelopment and also improves the quality of life for these children. Those receiving ARV treatment later, typically after 1 year, consequently respond more poorly in neurodevelopment and cognitive domains. It is therefore important that ongoing effort is placed on the initiation and management of ARV through the focus on early diagnosis, successful referral and maintenance in care (Porter, 2015). According to the literature, factors such as socio-economic barriers, misclassification of the HIV stage and insufficient awareness of the disease are common contributing factors for late ARV initiation (Jemmott et al., 2014; Kimani-Murage et al., 2013).

Whether patients were compliant or not in terms of ARVs was reported in 16 out of the 20 cases. The reasons for non-compliance reported in the results are consistent with reasons for non-compliance reported in the literature (Sendagala, 2010).

**Developmental history.** Developmental histories were not available for all of the children in the sample; hence proportions noted here may not represent the entire subsample.

For example, four of the children were noted to have been delivered prematurely, while 5 were carried to term. Although earlier studies concluded that HAART during pregnancy was associated with an increased risk of premature (e.g., Townsend, Cortina-Borja, Peckham, and Tookey, 2007), more recent studies have stated that in this era of increased ARV usage, there has been a decrease in the incidence of prematurity and low birth weight among HIV mothers (Schulte, Dominguez, Sukalac, Bohannon & Fowler, 2007; Shapiro et al., 2010). Given these discrepancies and the dearth of literature on the topic, future research should investigate the possible relationship between the HIV infection in mothers and ARV usage, and low birth weight and preterm births.

In the sample, 6 mothers reportedly consumed alcohol during pregnancy. According to Adnams (2010) within the South African context, fetal alcohol spectrum disorders (FASD) (which occur as a function of alcohol consumption during pregnancy) and HIV are commonly comorbid. However, a formal diagnosis of FASD was only reported in 1 and a suspected diagnosis in another 1 out of the 6 cases. What is concerning is that in most of the histories in
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which alcohol consumption during pregnancy was reported, this was generally described as
heavy drinking. Hence, FASD may well be under diagnosed amongst the participants.

With regards to smoking during the pregnancy, this was reported in 2 cases. Although
smoking during pregnancy can result in a higher risk of low birth weight and preterm birth
(Aliyu et al., 2013), this was not this case within this specific sample. The mothers who smoked
during pregnancy were not the same mothers who gave birth prematurely.

*Developmental milestones.* Early childhood is an important developmental stage which
can impact significantly on the child’s ability to reach their full potential (Engle et al., 2011).
Given the results, it is evident that children within this sample are lagging behind quite
substantially, developmentally. There are apparent delays across motor and language domains
which is typical within pediatric HIV (Cohen et al., 2015; Van Rie et al., 2007). This becomes
problematic as these milestones form the foundation of a child’s potential to thrive socially and
academically, and there are critical periods in which age-appropriate milestones should be reach
that will ensures a child’s normal development (Peterson, 2013).

**School History.** The children in the sample were all attending primary school at the time
of their assessments. The majority of the children (70%) had failed at least one grade or did not
complete a grade and recommendations for special needs schooling was quite common within
this sample. These academic difficulties that majority of the children in the sample face is no
surprise given the delays in neurodevelopment and cognitive performance for many of the
children, coupled with their poor socio-demographic backgrounds. Hence, children in the sample
tend to be delayed in school and thus perform much poorer than non-infected children (Walker et
al., 2011).

**Aim 3: Neuropsychological profile of HIV positive subsample**

Due to the effects that HIV has on a developing brain, neuropsychological impairments
are frequently reported in a number of cognitive domains

The attention and processing speed problems reported in the results are consistent with
the relevant literature (Cohen et al., 2015; Malee et al., 2011; Puthanakit et al., 2013; Van Rie et
al., 2007). This outcome is not surprising given the neuropathology of the HIV infection, which
affects cerebral cortex and white matter (Puthanakit et al., 2013).
Regarding language related impairments reported for the sample, in their review, Van Rie et al. (2007) found that children performed significantly poorer in expressive language than in receptive language (Wolters, Brouwers, Moss & Pizzo, 1995 as cited in Van Rie et al., 2007). A delay in language development (more so with expressive language) is a typical occurrence in children with HIV and this delay usually occurs before any noticeable abnormalities in neurological examinations or CNS imaging (Van Rie et al., 2007). Two possible reasons for these findings are put forward by the authors. First, that most of the children who acquired HIV vertically tended to come from lower socio-economic backgrounds, and low socio-economic backgrounds are usually associated with language delays and a less frequent use of expressive language. Second, that children with HIV are prone to ear infections which could affect hearing and can interfere with language development and functioning, as discussed earlier. Within the current sample, the clinicians overseeing the case reports place emphasis on interventions for verbal language ability in 45% of the cases, therefore it can be assumed that expressive language was poor.

Consistent with the literature, impairments in general intellectual functioning was also reported for the current sample. Hoare et al., (2012) tested the PIQ and VIQ (using the WASI battery) with HIV infected children and healthy controls in South Africa (n = 24). They concluded that the children infected with HIV performed significantly lower than control group, and that poor performance in general intellectual functioning becomes problematic as it leads to persisting academic problems or school failure as compared to the general population.

Regarding executive functions there seems to be two disparate ideas as to how children with HIV function within this domain. For example Van Rie et al. (2007) found that children with HIV generally have impairments with regards to specific executive functions including attentional flexibility and manipulating and monitoring working memory content. However Cohen et al. (2015) found that there is a small difference in performance between HIV infected and healthy children within this domain. This result was however with specific reference to the Trail Making Test (TMT), which tests visual attention and tasks switching. Likewise, in the current sample, children seemed to perform better on some executive function tasks (e.g., the
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Tower test, used to assess planning and frustration tolerance) compared to others (the Digits backward task measuring working memory).

The overarching term, executive functions, is an umbrella term for a variety of cognitive processes. Executive functions rely on the integrity of the frontal lobes and improvements in certain cognitive processes will be demonstrated upon the neurophysiological development of the prefrontal cortex, for which development continues into adulthood (Anderson, 2002). Therefore Puthanakit (2013) brings forth the argument that although affects the prefrontal cortex, consequences thereof may only be noticeable in late adolescence and young adulthood, when processes subserved by the prefrontal cortex become vital for optimal functioning. Children within this sample are preadolescent, therefore it could be argued that they have not reached the age in which these deficits are fully identifiable. Additionally Anderson (2002) states that aspects of executive functions may exhibit varying developmental trajectories, which adds to the complexity in understanding this domain.

Given the literature, one cognitive domain in which poor performance was expected was memory. Throughout the limited literature on HIV infection and memory in children specifically, the conclusion is that the memory is generally poor (Keller et al., 2004, Puthanakit, 2013; Smith et al., 2006; Van Rie et al., 2007). However, according to the neuropsychology reports consulted for the current study, children were generally performing in the average range, which appears to contradict what past literature has found. In terms of the overall impressions included in those reports, it was suggested that the memory problems reported for many children in the sample were in fact a function of attention problems and not pure memory problems per se.

Lyon and Krasnegor (1996) write an interesting chapter on the relationship between memory and attention with regards to learning. They analyzed tests that were done on rhesus monkeys and chimpanzees, who naturally have poor attention, and how training these animal’s attention led to a better performance in their memory which enhanced their learning (Lyon and Krasnegor, 1996).

By understanding the intimate relationship between attention and memory, one can understand how so-called ‘memory’ problems can in fact be a function of poor attention, which, as demonstrated by the results, is impaired for a number of children in the sample. These
attentional problems can interfere with a child’s ability to learn. Attention is regarded as a gateway function to cognition; hence if attention is impaired other cognitive functions may also appear impaired.

Consistent with this idea of attention rather than pure memory problems for the children in this current study, a recent study done by Cohen et al. (2015) also discussed the idea that children with HIV do not seem to have memory problems. The authors put forward that memory is a construct that is understudied in HIV-infected children, and that there seems to be an inference that since adults with HIV have memory problems, so will children with HIV too. This extrapolation is of course not feasible due to how the virus affects developing and mature brains (Cohen et al., 2015).

Becoming familiar with these cognitive deficits is essential as subtle impairments can have a knock on effect to more marked complications, which will affect future academic performances, occupational prospects and community participation of children infected with HIV (Cohen et al., 2015).

**Recommendations in the neuropsychology reports**

One of the frequent recommendations made in the neuropsychological reports was the placement of children in special needs schools. However, within the South African context there are a number of barriers that can hinder such placements in special needs schools. These include limited or lack of access to such resources and a lengthy procedure accessing such schools due to bureaucratic reasons or limited spaces in the available schools, (B. Daniels, personal communication, February 19, 2014 as cited in Dollman, 2014; Ladbrook, 2009; Mayfield & Homack, 2005; Taylor et al., 2003).

One of the other recommendations made (which could be directly linked to special needs schooling) was the intervention for verbal language skills (e.g., extending vocabulary, reading, writing and comprehension skills). Given that most aspects of schooling depend on language, the idea is that such intervention might improve children’s overall academic performance. Besides improving academic performance, Brackis-Cott, Kang, Dolezal, Abrams and Mellins (2009) argue that better language skills will enhance a child’s ability to understand their illness, which can lead to better adherence to their medication and act as a protective factor against risky sexual
activities as they become adolescents and young adults. Therefore language skills become pertinent in all spheres of their lives.

One of the final recommendations was to positively reinforce tasks within schooling systems if the tasks that the children are engaging in become to challenging. Little and Akin-Little (2008) state that finding age appropriate positive reinforces can yield positive results in a child continuing on a desired task.

**Limitations and future research**

This study was not without limitations. One of the main limitations was the sample size ($n=20$). Although the sample size began with $n=40$, the main focus was on children referred to the PNC for HIV-related difficulties. Given the sample size, the results and recommendations should be viewed with caution, as this information cannot simply be generalized to the general pediatric HIV population. Future studies of this nature will endeavor to include data over many more years thereby increasing the sample size.

Another limitation was missing data. Due to the nature of this study this is something to be expected. Many children with HIV are foster children and are orphaned therefore a lot of the descriptive data will be missing. Also, parents or guardians could not at times recall of the retrospective data asked about the in the history taking sessions at the PNC. Additionally with the neuropsychological tests, not all children do all of the same tests; therefore there will be data missing in that regard too.

In terms of future research, given the implications of this study suggesting that children with HIV do not seem to perform poorly with the cognitive domain of memory per se, future studies need to investigate this finding as incorrectly associated memory deficits can have serious implications for schooling, learning and interventions.

**Significance**

With locally obtained data on the demographic, neuropsychological, and other profiles of children with HIV, we are able to identify the specific areas of strengths and weaknesses of children in our local community which is of great significance when designing and implementing intervention strategies. Such information can help us determine not only who to target primarily, but also which areas to focus on first.
References


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HIV-related referrals to a local pediatric neuropsychology clinic: A 1-year demographic and neuropsychological profile


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http://dx.doi.org/10.1001/jamaoto.2014.267


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http://dx.doi.org/10.1007/s11904-010-0070-4


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http://dx.doi.org/10.1093/tropej/fmp072
Appendix A

Measures

The measures outlined below include a variety of subtests from standardized neuropsychological batteries, commonly used at the PNC. These tests will form the basis of the neuropsychological outcomes described.

**General Intellectual Functioning.** The Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) measures general intellectual functioning which is developed for individuals aged 6-89. This test battery includes four subtests: Vocabulary and Similarities, which together form the Verbal IQ and Block Design and Matrix Reasoning, which together form the Performance IQ. The Vocabulary subtest is used to assess a participants’ word knowledge and their language skills and the Similarities subtest to assess their construction of concepts and abstract reasoning (Wechsler, 1999). The Block Design subtest is used to assess perceptual organization and Matrix Reasoning to test nonverbal fluid reasoning (Wechsler, 1999). Test-retest reliability ranges from .92 to .95 for VIQ and PIQ subtests. Content validity of the WASI was demonstrated by inspecting IQ scales, which were comparable to the WASI subtests.

**Memory and learning.** The Children’s Memory Scale (CMS) is a battery designed to assess learning and memory functioning in children aged 5 to 16 years (Cohen, 1997). The Dot Locations subtest of this battery is used to assess visuospatial memory (through recalling positions of blue dots on a grid) in three phases: a learning phase, distractor phase with an immediate recall, and a delayed memory phase after 25-30 minutes (Cohen, 1997).

The reliability coefficients for this specific subtest range from .61 to .82 (Cohen, 1997)

The Wide Range Assessment of Memory and Learning (WRAML) is a test battery designed to test memory and learning in individuals aged 5-90. There is a verbal memory component to this battery which is used to test the same domain. The verbal memory component includes learning, delayed and recognition trials. Test–retest reliability coefficients for this battery range from .59 to .77 (Sheslow & Adams, 1990)

**Attention and Working memory.** The Numbers subtest of the CMS is used to assess a participants’ basic concentration (forward span) and working memory (backward span) (Cohen, 1997). Trials of digits of increasing length are read to participants and they are required to either
repeat the numbers as they are (forward span) or to reverse the order of the digits and then repeat them (backward span). The reliability coefficients for the forward component ranges from .71 to .73 and for the backward component from .66 to .82 (Cohen, 1997). Structure and content validity ranges from .06 to .96, for all ages (Cohen, 1997).

In the Test of Everyday Attention for Children (TEA-Ch), the Sky Search subtest is used to assess selective attention. The subtest involves participants locating target spaceship pairs amidst distraction (Manly et al., 1999) Test-retest reliability coefficients for this subtest range from .75 to .80

**Executive Functions.** The Inhibition subtest from a Developmental Neurocognitive Assessment (NEPSY-II) is designed for children aged 5-16 and is used to assess the automatic response and the ability to shift between responses (Korkman et al., 2007). There are two components (shapes and arrows) with 3 conditions (Naming, Inhibition and Switching) in each component. For the NEPSY-II battery, reliability coefficients range from .62 to .89 (Korkman et al., 2007) Content and structure validity were demonstrated by research done on clinical samples (Korkman et al., 2007)

The Tower subtest of the Delis–Kaplan Executive Function System (D-KEFS; Delis et al., 2001) is used to assess a participant’s spatial planning, rule learning and inhibition of impulsivity (Delis et al., 2001). This subtest requires the participant to arrange the discs on the pegs of a board in a specific order in as few moves as possible. The test-retest reliability coefficient for this subtest is .89 (Lowe & Rabbitt, 1998).

**Fine Motor Skills.** The Fingertip Tapping test of the NEPSY-II battery is used to assess sensorimotor skills. The test requires the participant to repeat a sequential finger movement, to perform rhythmic movements with their hands and to use a pencil to write rapidly and meticulously (Korkman et al., 2007).

**Processing Speed.** The Wechsler Intelligence Scale for Children – IV (WISC-IV) can be used to assess children aged 6 to 16 years (Wechsler, 2004). The Coding subtest, which forms part of this battery, is used to assess processing speed. Coding tests the ability to focus their attention in order to scan, differentiate and order visual information (Wechsler, 2004). Reliability was measured through internal consistency, test-retest stability, and inter-rater reliability and the
coefficients score for coding was .84 across all age groups. Validity was established by comparing the WISC-IV battery with the WAIS-II (Wechsler Individual Achievement Test II) and WPPSI-III battery (Wechsler, 2004).
Appendix B

Ethical approval from the Psychology Department

22 June 2016

REFERENCE NUMBER: PSV2016-021

Researcher Name: Naaila Davids and Limpho Mokoena
Researcher Address: Department of Psychology, University of Cape Town

Dear Ms Davids and Ms Mokoena

PROJECT TITLE: HIV-related referrals to a local pediatric neuropsychology clinic: A 1-year demographic and neuropsychological profile.

Thank you for your submission to the Department of Psychology Research Ethics Committee.

It is a pleasure to inform you that the Committee has granted approval for you to conduct the study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote your REFERENCE NUMBER in all your correspondence.

Yours sincerely

[Signature]

Associate Professor Lauren Wild
Acting Chair, Department of Psychology Research Ethics Committee
Appendix C

Ethical approval from faculty of Health Sciences

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7935
Telephone (021) 468 5626
Email: shurett.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanetics/forms

28 June 2016

HREC REF: 444/2016

Dr L Schrieff-Elsom
Psychology Department
2.10, Humanities Graduate School Building
Upper Campus

Dear Dr Schrieff-Elsom

PROJECT TITLE: A 1-YEAR DEMOGRAPHIC AND NEUROPSYCHOLOGICAL PROFILE OF CHILDREN REFERRED TO PAEDIATRIC NEUROPSYCHOLOGY AT RED CROSS WAR MEMORIAL CHILDREN’S HOSPITAL, FOR HIV-RELATED DIFFICULTIES (hons-candidate-L Mokoena & N Davids)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30th June 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanetics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator must obtain appropriate institutional approval before the research may occur.

The HREC acknowledge that the students’ Limplo Mokoena and Nailla Davids will also be involved in this study.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.

HREC 444/2016
Appendix D

Ethical approval from Red Cross War Memorial Children’s Hospital

Dr L Schrieff-Eison
Red Cross War Memorial Children’s Hospital

Dear Dr L Schrieff-Eison

APPROVAL OF RESEARCH

PROJECT TITLE: A 1-YEAR DEMOGRAPHIC AND NEUROPSYCHOLOGICAL PROFILE OF CHILDREN REFERRED TO THE PEDIATRIC NEUROPSYCHOLOGY CLINIC AT THE RED CROSS WAR MEMORIAL CHILDREN’S HOSPITAL (RXH), FOR HIV-RELATED DIFFICULTIES

It is a pleasure to inform you that approval is hereby granted to conduct the above-mentioned study at Red Cross War Memorial Children’s Hospital.

Yours sincerely,

Dr AS Booysen
Manager: Medical Services
Date: 05.07.16
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Appendix E

RHX Consent form

Enquiries: Susan Malcolm-Smith
Telephone: 021 650 4695
Fax: 021 650 4104

Departement van Gesondheid
Department of Health
iSebe lezaMpilo

NEUROPSYCHOLOGY CLINIC

RESEARCH, TEACHING AND TRAINING

Name of Child:

The Neuropsychology Clinic is part of a Regional Paediatric Neurology Service at Red Cross Children’s Hospital which is a teaching hospital with links to the University of Cape Town and is therefore involved in teaching, training and research in child neurology and neuropsychology. All information is treated in confidence. Patient anonymity is assured in any research.

I give permission for the assessment to be used for teaching, training or research purposes.

Signed: ..........................................................

Name ..........................................................

Parent / Guardian / Other (please state) ..........................................................

Date ..........................................................
Appendix F

Boxplots (Figure 5 to Figure 30) showing the descriptive statistical data for each subtest done testing each domain.

Attention

Figure 5. Boxplot of basic concentration (numbers forward).

Figure 6. Boxplot of selective attention (sky search time per target).
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**Figure 7.** Boxplot of selective attention (sky search targets).

**Figure 8.** Boxplot of selective attention (sky search attention).
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Language

![Boxplot of comprehension of instructions](image1)

*Figure 9.* Boxplot of comprehension of instructions.

Memory

![Boxplot of verbal memory learning (WRAML)](image2)

*Figure 10.* Boxplot of verbal memory learning (WRAML).
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Figure 11. Boxplot of verbal memory delayed (WRAML).

Figure 12. Boxplot of verbal memory recognition (WRAML).
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Figure 13. Boxplot of repetitions task overall.

Figure 14. Boxplot of sequence task.
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**Figure 15.** Boxplot of Dot locations visual memory learning (CMS).

**Figure 16.** Boxplot of Dot locations visual memory immediate (CMS).
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Figure 17. Boxplot of Dot locations visual memory delayed (CMS).

Processing Speed

Figure 18. Boxplot of processing speed (coding).
Executive functions

Figure 19. Boxplot of Executive functions (Tower total achievement score).

Figure 20. Boxplot of Executive functions (Tower move accuracy ratio).
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Figure 21. Boxplot of Executive functions (Tower rule violations).

Figure 22. Boxplot of Executive functions (Tower time per move ratio).
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Working memory

Figure 23. Boxplot of basic concentration (numbers backward).

General Intelligence

Figure 24. Boxplot of General intelligence (WASI FSIQ).
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Figure 25. Boxplot of General intelligence (WASI PIQ).

Figure 26. Boxplot of General intelligence (WASI VIQ).
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Figure 27. Boxplot of General intelligence (WASI Block design).

Figure 28. Boxplot of General intelligence (WASI Matrix reasoning).
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Figure 29. Boxplot of General intelligence (WASI Vocabulary).

Figure 30. Boxplot of General intelligence (WASI Similarities).
Appendix E

Bar graphs graphically representing the individual scores of the participants for each subtest within the domains being tested, when \( n \geq 10 \)

Attention

![Bar graph of basic concentration (numbers forward).](image)

**Figure 31:** Bar graph of basic concentration (numbers forward).

Memory

![Bar graph of verbal memory learning (WRAML).](image)

**Figure 32.** Bar graph of verbal memory learning (WRAML).
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Figure 33. Bar graph of verbal memory delayed (WRAML).

Figure 34. Boxplot of verbal memory recognition (WRAML).
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Figure 35. Bar graph of Dot locations visual memory learning (CMS).

Figure 36. Bar graph of Dot locations visual memory immediate (CMS).
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Figure 37. Bar graph of Dot locations visual memory delayed (CMS).

**Processing Speed**

Figure 38. Bar graph of processing speed (coding)
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Working memory

**Figure 39.** Bar graph of basic concentration (numbers backward).

**Figure 40.** Bar graph of General intelligence (WASI FSIQ).
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**Figure 41.** Bar graph of General intelligence (WASI PIQ).

**Figure 42.** Bar graph of General intelligence (WASI VIQ).
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**Figure 43.** Bar graph of General intelligence (WASI Block design).

**Figure 44.** Bar graph of General intelligence (WASI Matrix reasoning).
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**Figure 45.** Bar graph of General intelligence (WASI Vocabulary).

**Figure 46.** Bar graph of General intelligence (WASI Similarities)