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Attention and Concentration Functions in HIV-Positive Adolescents who are on Anti-Retroviral Treatment

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1. Declaration

This research project is submitted in partial fulfillment of the requirements for the degree of MA(Neuropsychology) by coursework and research report in the field of Neuropsychology in the Faculty of Humanities, University of the Witwatersrand, Johannesburg, April 2013.

I declare that this research report is my own, unaided work. It has not been submitted before for any other degree or examination at this or any other university.

The word count is 32,655.



Jessica Dawn Rice (née Fry)

09/04/2013

Date

2. Abstract

Approximately 11.5 million Human Immunodeficiency Virus (HIV)-positive individuals were living in South Africa in 2007, many of whom were infected via mother-to-child transmission. The current study aimed to compare the attentional and concentration functioning of 30 seropositive adolescents on managed anti-retroviral (ARV) programmes, with a comparable group of 71 seronegative adolescents. The results showed that the uncorrected errors on trial 1; self-corrected errors on trial 2; time taken, uncorrected and self-corrected errors on trial 3 of the Stroop Colour-Word Interference Test; and the errors on the Trail Making Test Part B were significantly poorer in the seropositive sample. The results also indicated that the clinical variations in the HIV-positive sample, including the age at which ARVs were commenced; duration of ARV treatment; World Health Organisation (WHO) stage at diagnosis; starting and current $CD4^+$ counts; and starting viral load, but with the exception of the current viral load, impacted significantly on test performance.

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- My colleagues, Urvashi Maganlal (née Chiba), Daniel Greenslade, Shona Fraser, Cindy van Wyk, Stephanie MacIlwaine, and Kelly Holland, who assisted with the assembling of the neuropsychological test battery, the data collection, and the data capture.
  - Urvashi Maganlal (née Chiba), part of the MA(Neuropsychology), 2012 programme, is the originator of the idea for the project. She has been involved in setting up meetings at the Rahima Moosa Mother and Child Hospital, liaising with the relevant people, and assisting with setting up the logistics of the research project. She has also been involved in the data collection of the HIV-positive and HIV-negative samples and scoring of the tests. She is investigating executive functioning in HIV-positive adolescents on anti-retroviral treatment. She will conduct the relevant statistical analyses to examine executive functions.
  - Daniel Greenslade, part of the MA(Neuropsychology), 2012 programme, is one of the original members of the research team. He was involved early on in the conceptualisation of the research. He has also been involved in the data collection of the HIV-positive and HIV-negative samples and scoring of the tests. He is investigating visuospatial functioning in HIV-positive adolescents on anti-retroviral treatment. He will conduct the relevant statistical analyses to examine visuospatial functions.
  - Shona Fraser, part of the MA(Neuropsychology), 2012 programme, is one of the members of the research team. She has been involved in the data collection of the HIV-positive and HIV-negative samples and scoring of the tests. She is investigating memory functioning in HIV-positive adolescents on anti-retroviral treatment. She will conduct the relevant statistical analyses to examine memory functions.
  - Cindy van Wyk, part of the MA(Neuropsychology), 2012 programme, is one of the members of the research team. She has been involved in the data collection of the HIV-positive and HIV-negative samples and scoring of the tests. She is investigating language functioning in HIV-positive adolescents on anti-retroviral treatment. She will conduct the relevant statistical analyses to examine language functions.
  - Stephanie MacIlwaine, part of the MA(Neuropsychology), 2012 programme, is one of the members of the research team. She has been involved in the data collection of the HIV-positive and HIV-negative samples and scoring of the tests. She is investigating motor

functioning in HIV-positive adolescents on anti-retroviral treatment. She will conduct the relevant statistical analyses to examine motor functions.

- Kelly Holland, part of the MA(Psychology), 2012 programme, is one of the members of the research team. She has been involved in the data collection of the HIV-positive and HIV-negative samples, scoring of tests, and capturing the data. She is investigating the overall neuropsychological profile in HIV-positive adolescents on anti-retroviral treatment.

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4. Dedication

I dedicate this manuscript to my loving husband, Mr. Robert Bruce Rice; and my parents, Mr. Nicolas Kingsley and Mrs. Helga Dorothea Fry. They have provided me with the most incredible support through an extremely busy year. I am truly grateful to my husband, Rob, for making this year of fulltime study possible for me.

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6. Introduction

The prevalence of the Human Immunodeficiency Virus (HIV) in South Africa is one of the highest in the world. An estimated 5.6 million people were living with HIV and/or Acquired Immunodeficiency Syndrome (AIDS) in South Africa in 2009 (UNAIDS, 2011). Furthermore, HIV and AIDS affect the children and adolescent members of society significantly: the prevalence of HIV is 17.8 percent amongst those aged 15 - 49, with older adolescents and younger adults being particularly affected (UNAIDS, 2010a; 2010b). HIV prevalence in children aged 2 - 14 years was 2.5 percent in 2008 (Shisana, Rehle, Simbayi, Zuma, Jooste, Pillay-van-Wyk, 2009).

It is generally agreed that patients in either the symptomatic stages of HIV infection or those in whom AIDS has already developed, exhibit deficits in a variety of cognitive domains (Evans, Mason, Leserman, Bauer, & Petitto**,** 2002). These deficits manifest as motor impairment; psychomotor slowing (Becker, Dew, & Lopez, 1997; Law et al., 1994; Llorente et al., 1998; Navia et al., 1986; Stern et al., 1998; Tross et al., 1998); working memory difficulties (Baddeley, 1990; Rabbitt, 1997); as well as executive dysfunction (Bartok et al., 1997; Castellon et al., 1998; Martin et al., 1995; Martin et al., 1999; Sahakian et al., 1995). Attentional functioning has been investigated and found to be worse in HIV-positive than HIV-negative individuals (Watkins et al., 2000). Specifically, HIV-infected persons show deficits in dual-task or divided-attention paradigm-based activities (Hinkin et al., 2000). Their medication regimen may also potentially confound the neuropsychological functioning of HIV-infected persons. The focus of the current research study was an investigation into attention and concentration in HIV-positive individuals.

HIV impacts many aspects of neurological development and cognitive functioning that are vulnerable to the effects of the HI virus and anti-retroviral (ARV) treatment; HIV-related neurocognitive deficits can range from subtle changes in attention and psychomotor processing to dementia. Whilst the association between HIV and cognitive functioning has been well documented in adult populations (Lawler et al., 2010; Melrose, Tinaz, Castelo, Courtney, & Stern, 2008; Singh et al., 2010; Toborek et al., 2005), fewer studies have explored the effects of HIV in paediatric populations. The results of these studies are inconclusive due to certain methodological issues such as small sample sizes, the broad age group of the population ranging from neonates to adolescents, as well as cultural influences on neuropsychological assessment (Govender, Eley, Walker, Petersen, & Wilmshurst, 2011; Koekkoek, de Sonneville, Wolfs, Licht, & Geelan, 2008; Sherr, Mueller, & Varrall, 2009; Wachsler-Felder & Golden, 2002). Consequently, results on neurocognitive profiles are often generalised across age groups despite the diverse group differences. In spite of these limitations, research has shown that there are various, common neuropsychological symptomatology in children living with HIV. In

school-going children, the first signs of neuropsychological involvement are usually declining academic performance, behavioural changes, psychomotor impairment with eventual progressive cognitive impairment and the emergence of pyramidal tract signs (Civitello, 2003).

In addition to the obstacles in understanding the interaction between HIV, ARVs and neuropsychological functioning as noted above, it is difficult to generalise findings from other studies to the South African context. This is due to the previously limited access to ARVs at and after birth in South Africa. Specifically, in countries such as North America, ARV administration was initiated and controlled from birth for seropositive neonates. However, in South Africa, policy decisions fuelled by fears of azidothymidine (AZT; which is an ARV) toxicity and the high cost of ARVs prior to 2004/5 prevented the rollout of ARV treatment in the public sector (Butler, 2005). Many children were only placed on ARV treatment based on the severity of their clinical symptomology and/or viral loads (Coovadia, 2009). A study has shown that children who were placed onto Highly Active Anti-Retroviral Therapy (HAART) only after presenting symptomatically showed greater neurocognitive deficits compared to children who were placed on ARVs from birth (Laughton et al., 2010). Thus, the age of starting HAART is an important predictor for neuropsychological outcome and has an impact on cognition (Smith, Adnams, & Eley, 2008). Currently, the children who acquired HIV perinatally prior to 2005 are now teenagers and this generation had a late start on ARVs; they were only placed on ARVs when they presented with clinical symptoms, their viral loads were significantly elevated and/or their $CD4^{+}$ counts were markedly low (Coovadia, 2009).

To understand the implications of HIV and ARVs on cognition in this group of HIV-positive adolescents, a large study (in which the present research is positioned) entitled "The Neurocognitive Profile of HIV-Positive Adolescents on Anti-Retroviral Treatment in Johannesburg, South Africa" was conducted. The aim was to examine whether and how the neurocognitive profile of young seropositive adolescents, who are currently on managed anti-retroviral programmes, differs from a seronegative contrast group, comparable based on demographic characteristics such as age, level of education and socio-economic status.

The intention of the current study was to examine the cognitive functions of attention and concentration, including an exploration of focused attention, which implies a measure of concentration or effortful, selective processing; and divided attention, which requires the ability to partial out attentional resources at the same time. These aspects of attention and concentration were examined in adolescents between the ages of 13 and 16 years living with HIV who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise and were compared to an equivalent contrast group of HIV-negative adolescents. Furthermore, the study attempted to elucidate which aspects, such as duration on ARV treatment, World Health Organisation

(WHO) stage at diagnosis, viral load, and $CD4^+$ count, have an impact on the neurocognitive outcome in the domain of attention and concentration.

The final aim of this research was to provide greater insight into the interactions that are under investigation: attention and concentration functions in HIV-positive adolescents on ARVs. Comparing the HIV-positive and HIV-negative groups will help to increase the validity of the findings of this research. The research may assist in determining various protective or risk factors for optimal attention and concentration functioning, such as socio-economic status, and/or the presence of HIV etc. This research may also contribute information that can be used to guide future rehabilitation programmes and to direct medical and educational professionals who are working with seropositive adolescents. In order to do so, this research report presents a brief theoretical introduction into the concepts of attention and concentration in relation to HIV infection and ARV treatment. The research report then outlines the results of the investigation and puts forward a brief discussion of the findings.

7. Theoretical and Conceptual Background

7.1 Literature Review

7.1.1 Background Information on HIV and AIDS

7.1.1.1 Basic Information on HIV and AIDS

The Human Immunodeficiency Virus (HIV) is a retrovirus, which leads to Acquired Immunodeficiency Syndrome (AIDS), a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Infection with HIV occurs by the transfer of or contact with blood, fluids that contain blood, semen, pre-ejaculatory fluid, vaginal fluid, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells (Centre for Disease Control; CDC, 2010; Weiss, 1993).

The four major routes of transmission are unprotected sexual contact with the interchanging of fluids such as blood, semen, pre-ejaculatory fluid and vaginal fluid; direct contact with infected blood such as in transplants, transfusions and sharing contaminated needles; breastfeeding by a woman infected with the virus; and transmission from an infected mother to her baby at birth via blood and/or fluids around the baby (perinatal transmission). There are other routes of transmission but these predominantly pose a problem for health care providers, including contact with cerebrospinal fluid (CSF) and fluids surrounding bone joints. Importantly, for transmission to occur, the infected fluids and blood must come into contact with a mucous membrane or damaged tissue, or be directly injected into the blood stream, such as from a needle or syringe. Screening of blood products for HIV has largely eliminated transmission through blood transfusions or infected blood products in the developed world (CDC, 2010; Weiss, 1993).

7.1.1.2 Mechanism of Action

HIV infects vital cells in the human immune system, such as helper T-cells (specifically $CD4^+$ T-cells), macrophages, and dendritic cells. The virus overrides the programming of these host cells and causes the manufacture of reverse transcriptase to convert the viral ribonucleic acid (RNA) into deoxyribonucleic acid (DNA; Ellis, Calero, & Stockin, 2009). In so doing, the viral DNA invades the host cell's genetic material and allows for virus replication. HIV infection leads to low levels of $CD4^+$ T-cells through three main mechanisms. Firstly, there is direct viral killing of infected cells. Secondly, there is an increased rate of apoptosis in infected cells. Thirdly, there is killing of infected $CD4^+$ T-cells by CD8 cytotoxic lymphocytes that recognise infected cells (Civitello, 2003; Ellis et al., 2009).

The fight between the HI virus and the immune system is continuous. The body responds to this onslaught through the production of more T-cells, which too become infected, and are killed by the virus. This fight may continue for up to ten years before the body eventually succumbs, apparently because of the inability to produce $CD4^+$ T-cells any longer. When $CD4^+$ T-cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections. The body becomes unable to ward-off even the weakest of organisms, such as bacteria and viruses other than HIV, which are not usually a problem. As the immune system becomes more and more damaged the individual may develop increasingly severe opportunistic infections and cancers, leading eventually to an AIDS diagnosis (AVERT, 2011).

The World Health Organisation (WHO) defines four stages of HIV disease in adults and adolescents. According to this classification system, Stage 1 of infection, which refers to primary HIV infection, generally lasts for a few weeks and it is often accompanied by a short duration of flu-like illness. In up to approximately 20% of individuals, the HIV symptoms are serious enough to consult a doctor, but the diagnosis of HIV infection is frequently missed. During Stage 1 there is a large amount of HIV in the peripheral blood and the immune system begins to respond to the virus by producing HIV antibodies and cytotoxic lymphocytes. This process is known as seroconversion. If an HIV antibody test is done before seroconversion is complete, then it may not be positive (AVERT, 2011).

Stage 2 refers to the clinically asymptomatic stage of HIV infection. Stage 2 typically lasts for an average of 10 years and, as its name suggests, the individual is free from major HIV-related symptoms, although there may be swollen glands. The level of HIV in the peripheral blood drops to very low levels, but individuals remain infectious and HIV antibodies are detectable in the blood; thus, antibody tests will show a positive result. HIV is not dormant during this stage; indeed, it is very active in the lymph nodes. A test is available to measure the small amount of HIV that escapes the lymph nodes. This test measures HIV RNA, which is HIV genetic material, and is referred to as the viral load test. This test has an important role in the treatment of HIV infection (AVERT, 2011).

Stage 3 refers to the symptomatic stage of HIV infection. Over time the immune system becomes severely damaged by HIV. This is thought to happen for three main reasons:

- The lymph nodes and tissues become damaged because of the years of activity;
- HIV mutates and becomes more pathogenic and more varied, leading to more immune system destruction; and
- The body fails to keep up with replacing the $CD4^+$ cells that are lost.

In HIV-infected individuals who are not receiving treatment or who are on treatment that is not working, the immune system fails and symptoms develop. Initially many of the symptoms are mild, but as the immune system deteriorates the symptoms worsen. Symptomatic HIV infection is mainly caused by the emergence of certain opportunistic infections that the immune system would normally prevent. This stage of HIV infection is often characterised by multi-system disease and infections can occur in almost all body systems. Treatment for the specific infection is often carried out, but the underlying cause is the action of HIV as it erodes the immune system. Unless HIV itself can be slowed down the symptoms of immune suppression will continue to worsen (AVERT, 2011).

Stage 4 refers to the progression from HIV to AIDS. As the immune system becomes more and more damaged, the individual may develop increasingly severe opportunistic infections and cancers, leading eventually to an AIDS diagnosis (AVERT, 2011).

The clinical criteria used by the WHO to diagnose the progression of HIV to AIDS, differs slightly between adults and children under the age of five. In adults and children aged 5 or over, the progression to AIDS is diagnosed when Pneumocystis Jirovecii Pneumonia (PCP), Tuberculosis (TB), Kaposi's Sarcoma (KS), Cytomegolavirus, Toxoplasmosis, Cryptococcosis, Non-Hodgkin's lymphoma, Varicella Zoster and/or Herpes simplex, which are all classified as WHO's clinical stage 4 conditions, is diagnosed and/or the $CD4^+$ count is less than 200 cells/mm^3 or a $CD4^+$ percentage of less than 15 is measured (AVERT, 2011). In children aged 36 - 59 months, diagnosis is based on having a $CD4^+$ percentage of less than 20 (WHO, 2007). In children aged 12 - 35 months, an AIDS diagnosis is based on having any stage 4 condition and/or a $CD4^+$ percentage of less than 20. In children younger than 12 months, an AIDS diagnosis is based on having a $CD4^+$ percentage of less than 25 (AVERT, 2011).

The way in which HIV causes neurocognitive impairment is not fully understood, but it hypothesised that it likely involves multiple processes, such as inflammatory damage to brain cells and blood vessels; vascular dysfunction related to metabolic abnormalities; and acceleration of age-related neurodegeneration. HIV enters the brain soon after initial infection, typically within the first several days, but it does not cause significant damage right away. The virus is able to cross the blood-brain barrier, which is meant to protect the central nervous system from toxins and other harmful agents. HIV does this by hiding in immune cells, known as monocytes. Lipopolysaccharides that are in the blood from bacteria that are released following the damage HIV does to the gut lining appears to make the blood-brain barrier more permeable , allowing more of the virus to cross the blood-brain barrier. Once inside the brain, HIV triggers an inflammatory response that further disrupts the barrier. HIV in the brain does not infect neurons directly. Instead, a small amount of HIV may enter cells designed to support the central nervous system, such as astrocytes and oligodendrocytes, but HIV

does not replicate and produce new virus within these cells. Instead, the primary target of HIV is specialised brain macrophages, called microglia, and other cells of the monocyte line, which is a type of immune cell that is produced in bone marrow. Once inside these long-lived cells, HIV may remain in a prolonged latent state. Rather than directly killing brain cells, as it does with $CD4^+$ T-cells elsewhere in the body, HIV exerts its detrimental neurological effects by setting off a cascade of inflammatory changes. Immune cells activated to fight the virus produce various cytokines, which are chemical messengers and include interferon-alpha and tumour necrosis factor-alpha. These in turn activate astrocytes and attract more immune cells to the battlefield. These chemicals also trigger the release and inhibit the removal of glutamate, an excitatory neurotransmitter that can overstimulate and, consequently, damage neurons. This pro-inflammatory cascade disrupts cellular communication channels and promotes damaging oxidative stress. Furthermore, HIV Tat and gp120 proteins released when the virus replicates appear to have direct neurotoxic effects. Additionally, gp120 inhibits neurogenesis. Examined on post mortem, brains of HIV-positive individuals show inflammatory changes, excessive accumulation of astrocytes, known as astrocytosis or gliosis; demyelination, loss of the protective insulation surrounding neuron axons; and build-up of amyloid precursor proteins. Atrophy and/or abnormalities are found in various brain regions and structures, including the basal ganglia, hippocampus, and corpus callosum. MRI scans of HIV-positive individuals have also shown that neurocognitive impairment was associated with atrophy of grey matter and abnormal white matter (The Body: The Complete HIV/AIDS Resource, 2009).

Everall et al. (n.d., as cited in The Body: The Complete HIV/AIDS Resource, 2009) examined post mortem results from nearly 600 HIV patients who had died since 1999, soon after the advent of combination ARVs. While only approximately 18% of examined brains showed typical HIV-related brain pathology, most exhibited some other type of abnormality, and only 22% were normal.

Using magnetic resonance spectroscopy, Navia et al. (n.d., as cited in The Body: The Complete HIV/AIDS Resource, 2009) found evidence of inflammation in people with HIV and loss of neurons in people with HIV Associated Neurocognitive Disorder. While there is some loss or death of neurons in the brains of people with HIV-related neurological disorders, a more typical finding is damaged neurons with their dendrites damaged, so that they can no longer receive neural impulses; this process is known as synaptic pruning. The fact that some neurons are injured rather than dead may explain why partial reversal of impairment may occur after starting ARVs. The end result of this assault on the brain is the spectrum of cognitive, including attention and concentration; motor; and psychological difficulties. The extent of the inflammatory response does not appear to be closely correlated with the amount of HIV in the brain. Thus, even among individuals receiving suppressive ARVs, low-level residual virus may be enough to maintain this neurotoxic environment and its associated impairment.

7.1.1.3 Epidemiology

HIV infection in humans is considered a pandemic by the World Health Organisation (WHO). Nevertheless, complacency about HIV may play a key role in HIV risk. From its discovery in 1981 to 2006, AIDS has killed more than 25 million people and currently, HIV infects about 0.6 percent of the world's population. In 2009, AIDS claimed an estimated 1.8 million lives, down from a global peak of 2.1 million in 2004 and, of these deaths, approximately 260,000 were children. A disproportionate number of AIDS deaths occur in Sub-Saharan Africa, retarding economic growth and exacerbating the burden of poverty. An estimated 22.5 million people (68 percent of the global total) living with HIV live in sub-Saharan Africa, which is also home to 90 percent of the world's 16.6 million children orphaned by HIV/AIDS (CDC, 2010).

The prevalence of HIV in South Africa is one of the highest in the world. It is estimated that 5.6 million people were living with HIV and AIDS in South Africa in 2009. This is the highest number of people in any country (UNAIDS, 2011). It is estimated that, in the same year, 310,000 South Africans died of AIDS-related causes, reflecting the vast number of lives that the country has lost due to AIDS (UNAIDS, 2010a; 2010b).

In South Africa, the HIV prevalence amongst those aged 2 years and older varies by province with the Western Cape at 3.8 percent and the Northern Cape at 5.9 percent being least affected. Mpumalanga, with15.4 percent and KwaZulu-Natal, with15.8 percent are at the upper end of the scale (Shisana et al., 2009). The estimated overall HIV prevalence rate is approximately 10.6 percent. The total number of people living with HIV in 2011 was estimated at approximately 5.38 million, with an estimated 16.6 percent of the adult population aged 15 - 49 years being HIV-positive (Statistics South Africa, 2011). HIV prevalence in children aged 2 - 14 years was estimated as 2.5 percent in 2008, whilst a 2009 survey states that there were 330,000 children between the ages of 0 - 14 years with HIV (UNAIDS, 2010a; 2010b).

Treatment with anti-retroviral drugs reduces both the mortality and the morbidity of HIV infection. Although anti-retroviral medication is still not universally available, expansion of anti-retroviral therapy programmes since 2004 has helped to turn the tide of AIDS deaths and new infections in many parts of the world. Intensified awareness and preventive measures, as well as the natural course of the epidemic, have also played a role (Greener, 2002; Palella et al., 1998). Nevertheless, an estimated 2.6 million people were newly infected in 2009 (Joint United Nations Programme on HIV/AIDS, 2010).

7.1.1.4 Prognosis

7.1.1.4.1 Prognosis of Adults

The rate of clinical disease progression varies widely between individuals and has been shown to be affected by many factors such as host susceptibility, immune function and co-infections, as well as which particular strain of the virus is involved (Morgan et al., 2002). Most untreated people infected with HIV-1 eventually develop AIDS. These individuals typically die from opportunistic infections or malignancies associated with the progressive failure of the immune system. HIV progresses to AIDS at a variable rate that is affected by viral, host, and environmental factors. Most people will progress to AIDS within 10 years of HIV infection: some will progress much sooner, and some will take much longer. Even after HIV has progressed to diagnosable AIDS, the average survival time with anti-retroviral therapy was estimated to be more than five years (Buchbinder, Katz, Hessol, O'Malley, & Holmberg, 1994; Collaborative Group on AIDS Incubation and HIV Survival, including the CASCADE EU Concerted Action, 2000; Schneider et al., 2005). Another author noted that in areas where it is widely available, the development of Highly Active Anti-Retroviral Therapy (HAART) as an effective therapy for HIV infection and AIDS has reduced the death rate from this disease by 80 percent, and raised the life expectancy for a newly diagnosed HIV-infected person to between 20 and 50 years (Lawn, 2004).

Without anti-retroviral therapy, someone who has AIDS typically dies within a year (Buchbinder et al., 1994; Collaborative Group on AIDS Incubation and HIV Survival, including the CASCADE EU Concerted Action, 2000; Schneider et al., 2005). This is supported by results from another study that argues that without anti-retroviral therapy, death normally occurs within a year after the individual progresses to AIDS. Most patients die from opportunistic infections or malignancies associated with the progressive failure of the immune system (Morgan et al., 2002). Another study reported that without treatment, the net median survival time after infection with HIV is estimated to be 9 - 11 years, depending on the HIV subtype, and the median survival rate after diagnosis of AIDS in resource-limited settings where treatment is not available ranges between 6 and 19 months (Lawn, 2004). However, as new treatments continue to be developed and because HIV continues to evolve resistance to treatments, estimates of survival time are likely to continue to change (Morgan et al., 2002).

7.1.1.4.2 Prognosis of Children and Adolescents

The prognosis of 111 children and adolescents (from 2.5 months to 19.5 years of age) infected with HIV was assessed by Krasinski, Borkowsky, and Holzman (1989). The case-fatality ratio was 32 percent, with 25 percent of subjects passing away within one year of developing an HIV-associated illness. Opportunistic infection was the most common AIDS-defining illness and the cause of death in

22 of the 35 children who died. Pneumocystis Carinii and Fungal Pneumonias had the worst prognosis, whereas Cryptosporidiosis infections had a better outcome.

7.1.2 Neuropsychological Implications of HIV and Anti-Retroviral Therapy (ART)

7.1.2.1 Neuropsychological implications of HIV

HIV is known to have an impact on cognition. The relationship between HIV and cognitive dysfunction has been examined in adult populations (Lawler et al., 2010; Melrose et al., 2008; Singh et al., 2010; Toborek et al., 2005). After the HI virus has infected the central nervous system, deficits in motor, cognitive and behavioural functioning present (Wachsler-Felder & Golden, 2002). Further, it is generally accepted that patients in the symptomatic stages of HIV infection (including AIDS) exhibit deficits in a variety of cognitive domains, such as executive skills and motor speed (Evans et al., 2002).

The most common HIV-related neurocognitive deficit appears to be psychomotor slowing. It is thought that this difficulty may underlie deficits in higher-order cognitive processes, such as associative cognitions (Becker et al., 1997). Psychomotor slowing may be evident even in the earliest stages of HIV infection (Stern et al., 1998; Law et al., 1994). Reaction time tasks have been helpful in detecting HIV-related cognitive slowing, since they offer a precise analysis of the effects of HIV on psychomotor processing (Hinkin et al., 2000).

Recent studies have found evidence of the impairment of verbal and spatial working memory processes in HIV-positive persons (Bartok et al., 1997; Martin et al., 1995; Martin et al., 1999; Sahakian et al., 1995). It is hypothesised that this is due to the affinity of the HI virus for frontal–subcortical circuits. Given the involvement of frontal and subcortical structures in HIV infection, executive processes (including working memory) are affected. Deficits of working memory tend to be observed in the later stages of HIV infection or AIDS (Castellon et al., 1998).

Depression, anxiety, and substance abuse are conditions seen in HIV disease that may contribute to neurocognitive impairment, including attention and concentration difficulties (Fernandez, Levy, & Ruiz, 1994). Other factors may potentially confound the neuropsychological functioning of HIV-infected persons. These include gender, ethnicity, level of education, low socio-economic status and medication regimen (Fernandez et al., 1994).

There are fewer studies that have investigated the effects of HIV in paediatric and adolescent populations than in adult populations (Govender et al., 2011; Koekkoek et al., 2008; Sherr et al., 2009; Wachsler-Felder & Golden, 2002). The research that has been conducted in paediatrics and adolescents has shown that there are various, common, neuropsychological symptomatology in

children living with HIV: HIV-related cognitive deficits can range from subtle changes in attention and psychomotor processing to dementia (Civitello, 2003).

Clinical symptoms of primary infection are diffuse rather than focal (Koekkoek et al, 2008). Radiological studies with seropositive children have revealed cortical atrophy and calcification, especially in the basal ganglia and frontal cortex white matter (Belman et al., 1985; Belman et al., 1986; Civitello, 2003; Epstein, Berman, Sharer, Khademi, & Desposito, 1987), as well as myelinopathy. Thus, one can assume that HIV affects neurodevelopment in seropositive children once the virus has infected the central nervous system (Gay et al., 1995).

For the most part, studies on the effects of HIV in children have emerged from the United States of America (USA) and Europe focusing on the clade B strain of HIV (Koekkoek et al, 2008; Tardieu, 1998; Wachsler-Felder & Golden, 2002). A study from the USA showed that anti-retroviral-naïve children who were placed onto HAART after presenting symptomatically showed greater neurocognitive deficits when compared to children who were placed on ARVs from birth (Laughton et al., 2010).

A recent study that was conducted in Thailand examined the specific neurocognitive profile of school-aged, perinatally-acquired HIV-positive children (with the clade E strain, which is the most virulent strain of HIV) who had limited access to ARV treatment at and after birth as a consequence of the high cost of ARVs. The authors also examined the neurocognitive change after receiving ARVs. A prospective cohort study of HIV-infected Thai children from 6 – 12 years of age compared with HIV-affected (children of HIV-positive mothers who were not infected with HIV), and normal control groups was conducted. The Wechsler Intelligence Scale for Children – III (WISC-III; Wechsler, 1991) was administered at enrollment and then again 30 months later, at follow-up. Semi-structured interviews with the primary caregivers were performed. One hundred and twenty one (121) children were enrolled of which 39 were HIV-infected, 40 were HIV-affected (individuals whose lives are directly influenced by HIV infection), and 42 were control children with a median age of 9.3 years. The HIV-infected group had a mean $CD4^+$ percentage of 13.8. Further, 87 percent of the HIV-infected group had been receiving ARVs for a median of 35 weeks (Puthanakit et al., 2010).

At the first cognitive assessment, the mean full-scale intelligence quotient (FSIQ) was 79 and 88 amongst HIV-infected and HIV-affected children respectively. These results were significantly lower than the control group at 96 ($p < .01$). At follow-up 30 months later, the HIV-infected group had a mean $CD4^+$ percentage of 25.6 and 77 percent had undetectable viral load. The mean FSIQ of the children in the three groups was 75, 85, and 91, respectively. Compared with the baseline assessment, the results indicated that the verbal scale score significantly decreased in all groups, including the

controls, whereas the performance scales did not change. The authors concluded that school-aged HIV-infected children have lower cognitive function than HIV-affected and normal children. Furthermore, cognitive function was not improved after receiving ARVs (Puthanakit et al., 2010).

In the developing brains of infants, a characteristic feature of HIV infection is impaired brain growth resulting in secondary microcephaly with onset between two and four months of age. This post-natal period of brain development is especially vulnerable to excite-toxic neuronal injury, due to the active synaptogenesis and pruning that takes place at this age associated with over-expression of excitatory amino acid (EAA) receptors. HIV infection of microglia and perivascular macrophages in the brain results in chronic inflammation, which manifests pathologically as diffuse microglial activation and reactive astrogliosis. Several inflammatory products of activated microglia, which includes tumor necrosis factor alpha (TNF-alpha) and platelet-activating factor (PAF), have been found to act as neuronal toxins. This toxic effect can be antagonised by blocking NMDA (or AMPA) glutamate receptors, suggesting that (weak) excite-toxicity leads to oxidative stress, neuronal injury, and apoptosis. HIV infection and chronic inflammation may also contribute disruption of the blood-brain barrier and could result in further entry into the central nervous system (CNS) of toxic viral, cellular products, or additional HIV-infected cells. It has been hypothesised that prolonged microglial activation during HIV infection underlies the neuronal injury and impaired brain growth in affected infants. Further investigation of the interaction between HIV-infected/activated microglia and developing neurons seems warranted. The current understanding of HIV neuropathogenesis implies that therapeutic strategies should target the sustained immune activation in microglia, attempt to repair the integrity of the blood-brain barrier, and provide neuroprotection from excite-toxic neuronal injury (Epstein & Gelbard, 1999).

7.1.2.2 The Neuropsychological Implications of ARVs

HAART has been shown to produce beneficial effects on neurocognitive functioning in HIV-infected women with severely impaired immune systems. The greatest benefits were reported for women who had received HAART for more than 18 months (Cohen et al., 2001). However, poor neuropsychological functioning has been demonstrated for HIV-infected children and this was worse for children with higher viral loads. Only one measure of neuropsychological functioning showed improvement after treatment with combination therapy, and the extent of that improvement was relatively minor. The authors concluded that treatment strategies for children with HIV disease need to be re-evaluated so that treatment strategies can consider restoration of neuropsychological functioning in addition to lowering the viral load (Jeremy et al., 2005).

Advanced age is associated with higher rates of anti-retroviral adherence; however, older participants who were cognitively impaired showed disproportionate difficulty in adequately adhering to their

medication regimen (Hinkin et al., 2004). Adherence to ARVs is very important not only for overall health, but also as a neurocognitive protective factor; however, the interaction between adherence and cognitive performance can be complex. This is because people with cognitive difficulties find adhering to long-term treatments harder. Specifically, measures of cognitive functioning and depression severity were supported as predictors of objective measures of treatment adherence (Mackin &Areán, 2007). Furthermore, people with difficulties in ARV adherence may be at risk for higher cognitive deficits. Medication adherence has been increasingly recognised as an important factor in elderly persons' health. In a previous study, it was found that adherence predicted cognitive status at later time points, whilst cognition did not, in general, predict adherence. The authors suggested that interventions to ensure high levels of medication adherence may be important for maintaining cognitive function in affected elderly people (Ownby, Hertzog, & Czaja, 2012).

7.1.2.3 The Impact of HIV and ARVs on Attention and Concentration

7.1.2.3.1 A Brief Theoretical Review of Attention and Concentration Functions

The term attention can refer to a general level of alertness or vigilance; a general state of arousal; orientation versus habituation to a stimulus; the ability to focus, divide or sustain mental effort; the ability to target processing within a specific sensory arena; or a measure of capacity (James, 1890). In the past it was contested whether the term 'attention' implied a general state of cortical tone, or whether it referred to a set of specific structures or networks within the brain. Current views of attention hold that it is a multi-faceted concept that implies multiple behavioural states and cortical processes that various anatomical structures control (Zilmer & Spiers, 2001).

Under the umbrella term of attention, there are several divisions or characterisations. The first of these is focused attention, which refers to the ability to respond to and pick out salient information from a background of irrelevant external and internal stimuli. Focused attention also implies a measure of concentration or effortful processing (Cherry, 1953). The second division is alternating attention, which refers to the ability to alternate attention or switch back and forth, often rapidly, between different tasks. The third division is known as divided attention and this term refers to the ability to partial out attentional resources concurrently, rather than switching rapidly back and forth. The fourth division is sustained attention or concentration, which is the ability to maintain an effortful response over time; this is related to the ability to persist and sustain a level of vigilance (Sohlberg & Mateer, 1989).

Neuropsychological theories of attention usually consider the role of the reticular activating system (RAS) in cortical arousal; subcortical and limbic structures, including the cingulate gyrus, in the regulation of information to be attended to; the posterior parietal lobe system in focusing attention; and the frontal lobe in directing attention. Researchers have recognised the role of the basal ganglia

for their participation in the sensory selection of material for further attentional processing (Zilmer & Spiers, 2001). The right hemisphere of the brain is prominent as an attentional processor. The reticular formation (RF) has been found to have a role in regulating levels of cortical activation and arousal. The pulvinar nucleus of the thalamus, the posterior parietal cortex, the inferior parietal, superior temporal cortices, the cingulate cortex and the frontal lobes play a role in focused and selective attention. Sustained attention is controlled by the right fronto-parietal-thalamic network. The noradrenergic pathway is involved. Divided attention is controlled by the anterior cingulate cortex, dorsolateral prefrontal cortex and the areas of the specific sensory modality (e.g. visual cortex). Alternating attention is controlled by the posterior parietal lobe (attention to spatial target), the superior colliculus (saccading eye movements bringing peripheral stimuli into foveal vision), and the pulvinar nucleus (filter). Alternating attention is influenced by the cholinergic system. Effortful attention is controlled by the anterior cingulate cortex, the lateral prefrontal cortex (plus the supplementary motor area), the orbitofrontal cortex, the dorsolateral prefrontal cortex, the basal ganglia and the thalamus. The ability to encode information involves the hippocampus and the amygdala. The noradrenergic and acetylcholine systems and predominantly the dopamine systems are involved. Theorists have not elucidated a one-to-one correspondence between levels of attentional behaviour and brain structures or networks. Rather, subsets of brain systems related to attention are described (Mesulam, 1985; Posner & Petersen, 1990).

7.1.2.3.2 Use of the Various Neuropsychological Tests as Measures of Attention and Concentration

There are various neuropsychological tests which can be used to measure each category of attention, including verbal and visual focused attention, and verbal and visual divided attention. These tests include the time taken and the number of errors made on the Stroop Colour-Word Interference Test (Golden, 1978; Moering et al., 2003), the time taken and the number of errors made on the Trail Making Test (Army Individual Test Battery, 1944), trials A1 and B1 of the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996; Senior, 2000), the Wechsler Intelligence Scale for Children – Revised (WISC-R; Wechsler, 1974) Digit Span subtest, the WISC-R Picture Completion subtest, and the number of failures to maintain set on the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993; Milner, 1963). In previous studies, these measures have been shown to tap into attentional functioning (Busse & Whiteside, 2012; Christidi, Zalonis, Smyrnis, & Evdokimidis, 2012; Davidson, Zacks, & Williams, 2007; Fuentes et al., 2003; Greve, Williams, Haas, Littell, & Reinoso, 1996; Lansbergen, Kenemans, & van Engeland, 2007; Massman, Nussbaum, & Bigler, 1988; Oades, Röpcke, Henning, & Klimke**,** 2005; Riccio et al., 2009; Savitz & Jansen, 2003).

In terms of the Stroop Colour-Word Interference Test, a meta-analysis of 19 studies revealed more interference for Attention Deficit Hyperactivity Disorder (ADHD) groups relative to the control groups. The authors concluded that interference control, as measured by trial 3, is consistently

compromised in individuals with ADHD, likely due to attention deficits (Lansbergen et al., 2007). In a similar study, the performance on the Stroop Colour-Word Interference Test by 36 boys with a diagnosis of ADHD was poorer than a control group on both the control (trials 1 and 2) and the interference (trials 3 and 4) conditions of the test (Savitz & Jansen, 2003). The fundamental feature of the ADHD group was attention deficit, and this was thought to underlie their poorer performance on the Stroop Colour-Word Interference Test. In a separate study, it was noted that older adults show a greater increase in the number of errors made in the naming of print colours of the incongruent colour of words (trial 3 of the Stroop Colour-Word Interference Test) than do younger adults. This was attributed to attention difficulties and the general slowing effects of age in older adults and to age deficits in inhibition and frontal lobe dysfunction (Davidson et al., 2007). Thus, the Stroop Colour-Word Interference Test has been shown to be an adequate measure of attention.

Regarding the Trail Making Test, a previous study evaluated the classification accuracy of a commonly used attention/concentration measure, namely, the time taken on the Trail Making Test. Participants included 413 individuals who completed a comprehensive neuropsychological evaluation. Classification accuracy on the Trail Making Test Part B (.75) was acceptable; however, classification accuracy on the Trail Making Test Part A (.62) was poor. Given that the sensitivity rate was not adequate for the Trail Making Test Part A, there remains a need to utilise highly sensitive measures in addition to these embedded measures (Busse & Whiteside, 2012). Thus, the Trail Making Test Part B, but not Part A, has been shown to be an adequate measure of attention.

Pertaining to trials A1 and B1 of the RAVLT, a study was conducted to investigate selective attention in amyotrophic lateral sclerosis (ALS) patients and to examine the contribution of selective attention to the patients' verbal free recall on these trials. The authors examined 22 non-demented patients with sporadic ALS and 22 demographically-related controls. Selective attention was found to influence immediate verbal free recall on the RAVLT (Christidi et al., 2012). Thus, this test has been shown to be an adequate measure of attention.

In terms of the WISC-R Digit Span subtest, the relationship between ADHD and test performance was examined. Hyperactivity/attentional problems were measured by the Hyperactivity Scale of the Child Behaviour Checklist. Performance on a neuropsychological task thought to contain an attentional component, the WISC-R Digit Span subtest, was used to operationalise attention. For children of between 9 and 12 years of age, there were significant, and largely negative, correlations between hyperactivity scores and neuropsychological test scores. Thus, the results indicated that hyperactivity/inattention has an effect on test performance, specifically, the number of digits correctly repeated and reversed (Massman et al., 1988).

Regarding the WISC-R Picture Completion subtest, a study investigated some cognitive functions in relation to the overall state of monoamine activity in patients with schizophrenia. Profiles of the relations of the activity of dopamine, noradrenaline and serotonin to neuropsychological dysfunction in major patient sub-groups, with their very different cognitive characteristics, have not been reported. Serum measures of dopamine, noradrenaline and serotonin turnover were examined, by regression analyses, for the prediction of performance on neuropsychological measures in 108 patients with schizophrenia and 63 matched controls. Paranoid and non-paranoid subgroups were based on ratings from the Positive and Negative Syndrome Scale (PANSS). Right-sided cerebral function, as investigated with the Picture Completion subtest, was sensitive to the relative activities of the monoamines: low dopaminergic activity predicted poor attentional set control in those participants with ideas of reference (Oades et al.**,** 2005). Additionally, in a separate study, seven year old children were administered the WISC-R Picture Completion subtest. The results of this study suggested that this test is sensitive to attention in school children (Fuentes et al., 2003).

Pertaining to the WCST, a previous study examined attention functions in children with ADHD using the WCST. The purpose of this study was to explore the relationship between performance on the WCST and cognitive ability. Notably, none of the results of the WCST were found to correlate with attention (Riccio et al., 2009). In contrast to this, a separate study sought to test the hypothesis that the failure to maintain set score on the WCST reflects attentional function. Support was shown for the suggestion that this score reflects attentional dysfunction (Greve et al., 1996). This indicates that the WCST may be an adequate measure of attention.

Thus, the various neuropsychological measures, including trials A1 and B1 of the Rey Auditory Verbal Learning Test (RAVLT), the time taken and the number of errors made on the Stroop Colour-Word Interference Test, the time taken and the number of errors made on the Trail Making Test, the WISC-R Digit Span subtest, the WISC-R Picture Completion subtest, and the number of failures to maintain set on the WCST have been shown to assess attentional functioning.

7.1.2.3.3 Deficits in Attention and Concentration related to HIV and ARVs

HIV infection has been associated with deficits in attention (Law et al., 1994; Martin et al., 1992; Sorenson, Martin, & Robertson, 1994). It has been argued that cognitive slowing may be at the root of the attentional deficits seen in many symptomatic persons (Sorenson et al., 1994). Unfortunately, cognitive slowing tends to worsen with increasing disease severity, which has a knock-on effect on attention functioning. However, according to Hardy and Hinhn (2002), a significant percentage of studies failed to find that HIV infection leads to reaction time slowing. For this reason, the actual infection with HIV must account for some of the evident cognitive decline in adults. The characteristic neuropsychological symptomatology of infected adults includes memory dysfunction,

higher order attentional disturbance, executive dysfunction and cognitive slowing (Hardy & Hinhn, 2002).

Singh (2009) notes that neurocognitive impairment occurs in 10 - 60 percent of people living with HIV/AIDS, depending on the stage of the disease. People with HIV-associated neurocognitive disorder have impairment on multiple cognitive domains, including attention, concentration, memory, executive function, motor functioning and speed of information processing, and sensory perceptual/motor skills deficits. The milder forms of HIV-associated neurocognitive disorder are easily missed. Diagnosis can be made on clinical grounds in the most severe cases; however, milder forms and confirmation of the diagnosis require neuropsychological testing.

HAART has led to a 40 percent decline in the incidence of HIV dementia. In the post-HAART era, HIV dementia runs a more chronic course, is milder and is reversed in about a third of cases. However, HAART is not universally successful because incident cases occur in people on HAART. Overall HAART has been shown to be of benefit, and screening for HIV-associated neurocognitive disorder should be the standard of care for people living with HIV/AIDS. HIV dementia is an AIDS-defining illness and patients should qualify for HAART irrespective of their $CD4^+$ count. However, the benefit of starting ARVs for people with asymptomatic neurocognitive impairment and minor neurocognitive disorder, including difficulties with attention and concentration, is currently inconclusive (Singh, 2009).

Attentional functioning has been investigated and found to be worse in HIV-positive than HIV-negative children (Watkins et al., 2000). Specifically, HIV-infected children show deficits in divided-attention activities (Hinkin et al., 2000). Importantly, scant research has been conducted into the effects of HIV on attention and concentration in adolescents. In this regard, the research that has been conducted has tended to focus more on either children or adults, but not on adolescents (Watkins et al., 2000).

A study was conducted on adolescents where attentional functioning was examined in 7 to 19 year old male HIV-positive and HIV-negative participants. Two measures sensitive to attention deficits were used: the Continuous Performance Test (CPT) and the Span of Apprehension. On the CPT, there was a decrement in attention in the HIV-positive group that was not present in the HIV-negative group (Watkins et al., 2000). Thus, HIV appears to affect attentional functioning in adolescents.

In conclusion, the findings of the various research studies are fairly consistent in acknowledging the impact that HIV and ARVs have on attention and concentration. Some studies have argued that cognitive slowing may be at the root of the attentional deficits, whilst others hold that these symptoms

are due to the effects of the virus itself. Research into the benefits of starting ARVs for people with minor neurocognitive disorder, including difficulties with attention and concentration, is inconclusive.

7.1.2.3.4 Deficits in Attention and Concentration related to HIV Clinical Variations

Various clinical data of HIV-positive individuals, including the age at which HAART was commenced, the duration of ARV treatment, the WHO stage at diagnosis, the starting and current $CD4^+$ cell counts, and the starting and current viral loads, have been found to impact significantly on attention and concentration. Specifically, a previous study examined the association between participants' recent trends in $CD4^+$ cell counts and viral loads and cognitive test performance. Eighty three (83) HIV-infected patients with a mean $CD4^+$ cell count of 428 copies/mm^3 were examined. The authors investigated the relationships between $CD4^+$ cell counts, one-year trends in immunologic function, and cognitive performance. One-year clinical history for $CD4^+$ cell counts was predictive of attention difficulties. Models that combined recent clinical history trends and $CD4^+$ cell counts suggested that recent clinical trends were more important in predicting current cognitive performance. This research suggested that recent $CD4^+$ cell count and viral load history is an important predictor of current cognitive function across several cognitive domains, including attention and concentration (Tate et al., 2011).

Another study hypothesised that performance on measures of attention, including the Trail Making Test Parts A and B, the Stroop Colour-Word Interference Test, and the Digit Symbol Coding Test, would be affected by HIV clinical variables such as $CD4^+$ and HIV RNA levels, duration of illness, anti-retroviral treatment and plasma cytokine concentrations. Cohen et al. (2011) studied 64 adults including 37 men and 27 women, 30 of whom were HIV-positive, while 34 were HIV-negative. The duration of HIV infection ranged from 2 to 26 years. Performance on the neurocognitive measures was found to be associated with cytokine concentrations; cytokine concentrations were amongst the strongest predictors of neurocognitive function relative to other clinical factors. The authors argued that their findings also pointed to the potential value of simultaneously examining a panel of different biomarkers. This is because a complex relationship likely exists amongst cytokines and that these relationships are mediated not only by HIV infection, but also by anti-retroviral treatment and other comorbid conditions (Cohen et al., 2011).

In a separate study, it was noted that there is some controversy regarding the importance of viral load in mediating neurologic disease and its effects on cognition, including attention. However, the current viral load was found to be important in that study. The authors used RNA assays to examine the HIV viral load in the plasma and the CSF in brains from ten autopsied HIV-infected subjects and two non-infected controls. Their findings were that the HI virus was not uniformly distributed throughout the brain. Selective regions, including the basal ganglia and the hippocampus, showed higher levels of

virus than the cerebellar cortex and mid-frontal cortical gray matter. The authors held that the disruption of these subcortical structures, and the subsequent impact on the subcortical-cortical pathways, would lead to difficulties in attention (Wiley et al., 1998).

Thus, the findings of the various research studies are fairly consistent in acknowledging the impact that the various clinical variations in HIV-positive individuals have on attention and concentration. Additionally, scarce research has been conducted into the functioning of attention and concentration in adolescents: research conducted has tended to focus more on children and adults.

7.2 Rationale

The prevalence of HIV in South Africa is one of the highest in the world (UNAIDS, 2011). Furthermore, HIV and AIDS significantly affect the younger members of our society, including children and adolescents: the prevalence of HIV is 17.8 percent amongst those aged 15 - 49, with older adolescents and young adults being particularly affected (UNAIDS, 2010a; 2010b). HIV prevalence in children aged 2 - 14 years was 2.5 percent in 2008 (Shisana et al., 2009). Thus, HIV is a major issue in the South African context.

HIV and ARVs impact many aspects of cognitive functioning. Specifically, HIV-related neurocognitive deficits can range from subtle changes in attention and psychomotor processing to dementia. Objective impairments in HIV include psychomotor slowing, forgetfulness, and difficulties with attention and concentration. In the later stages of HIV infection (including symptomatic HIV and AIDS), executive skills and motor speed may also become impaired (Evans et al**.,** 2002). Further, research has shown that there are various, common neuropsychological symptomatology in children living with HIV, including declining academic performances, behavioural changes, psychomotor impairment with eventual progressive cognitive impairment and the emergence of pyramidal tract signs (Civitello, 2003).

The interactions between HIV, ARVs and cognition appear to be complex. However, from the literature, it seems that the earlier treatment is commenced, the less cognitive impairment is evident. The age of starting HAART is an important predictor for neuropsychological outcome and has an impact on cognition (Smith et al., 2008). A study has shown that children who were placed onto HAART only after presenting symptomatically, showed greater neurocognitive deficits compared to children who were placed on ARVs from birth (Laughton et al., 2010). However, due to political reasons, such as fears of ARV toxicity and the high cost of ARVs, prior to 2004/5 there was a situation of limited access to ARV treatment at and after birth for the children who acquired HIV perinatally in South Africa. Thus, policy decisions prevented the rollout of ARV treatment in the public sector (Butler, 2005) and many children were only placed on ARVs based on the severity of

clinical symptomology, such as encephalitis, tuberculosis and/or pneumonia, and/or high viral loads (Coovadia, 2009). By then, some central nervous system functionalities may have already been compromised in this group of children. Unfortunately, the picture becomes more complex when issues which are particular to South Africa, such as poverty, quality of education, and access to health services, are taken into account. This then justifies the use of an HIV-negative contrast group for this study.

The present research attempted to understand the interactions between variables relating to HIV and ARVs, and demographic characteristics, as well as the impact on attention and concentration. Scant research has been conducted into the effects of HIV on attention and concentration in adolescents: research conducted has tended to focus on children and adults, but not adolescents (Watkins et al., 2000). The attempt to understand the interactions between attention, concentration, HIV, ARVs, and demographic characteristics is relevant in order to provide insight into the neuropsychological profile of attention and concentration in HIV, as well as the implications on education, health and policy making that this may have. The present research aims to answer the following question:

7.3 Research Question

What are the characteristics of attention and concentration in a sample of HIV-positive adolescents, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, in comparison with an equivalent sample of HIV-negative adolescents, both study groups between the ages of 13 and 16 years old?

Are the particular aspects of the selected neuropsychological tests that were utilised in the current research project correlated with the respective attention and concentration functions that they are purported to assess?

8. Method

8.1 Research Aims

8.1.1 General

The comparison of the attention and concentration functions between adolescents in the age group of 13 to 16 years living with the Human Immunodeficiency Virus (HIV) who were commenced on managed anti-retroviral (ARV) programmes following diagnosis of HIV and immune compromise against an equivalent contrast group of HIV-negative adolescents.

8.1.2 Specific

To describe the attention and concentration functions of adolescents with HIV on managed ARV programmes.

The comparison and/or identification of group differences of attention and concentration functions between adolescents with HIV who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise and a contrast group of HIV-negative adolescents.

8.2 Research Design

8.2.1 Independent Variable

8.2.1.1 HIV Status

8.2.1.1.1 Conceptual Definition

A person's HIV status can take one of two values: HIV-positive or HIV-negative.

HIV-positive status is the presence of the HI virus, the HIV antibodies and the HIV antigens identified by using tests such as the enzyme-linked immunosorbent assay (ELISA), the Western Blot or Rapid Tests, and/or HI virus antigen tests.

HIV-negative status is the absence of the HI virus, the HIV antibodies and the HIV antigens.

8.2.1.1.2 Operational Definition

In the HIV-positive sample, the presence of the HI virus, HIV antibodies and/or HIV antigens had been diagnosed using standard medical tests, such as ELISA, Western Blot or Rapid Tests, and/or HI virus antigen tests, by a general practitioner and/or other medical doctor or health care practitioner. The researchers had access to the participants' medical files to confirm the HIV-positive diagnosis.

Given the sensitive nature of an HIV-positive diagnosis, as well as the fact that HIV/Acquired Immunodeficiency Syndrome (AIDS) is not a notifiable disease, the researchers were not ethically, or legally, permitted to directly question the individuals' HIV status. Where possible, this information was deduced in the HIV-negative sample through questions answered by the teachers at the Sowetan school regarding chronic medication; the individuals in this sample were not taking anti-retroviral medication. Furthermore, where possible, the seronegative status was elucidated based on questions answered by the teachers at the school regarding the overall rate of absenteeism from school of each of the potential candidates, which was taken to indicate the current absence of HIV-related secondary infections.

8.2.2 Dependent Variables

8.2.2.1 Attention and Concentration Functions

8.2.2.1.1 Conceptual Definition

Attention is the cognitive process that allows individuals to orient to, select and maintain focus on information to make it available for cortical processing. Attention is a multifaceted concept that involves multiple cortical processes and behavioural states. Within the specific sensory arenas of visual and verbal attention, there are two further categories. Focused attention implies a measure of concentration or effortful processing. Divided attention requires the ability to partial out attentional resources at the same time (Zilmer & Spiers, 2001).

8.2.2.1.2 Operational Definition

Each category and modality of attention was understood as the data that resulted from the scores on the following neuropsychological tests:

- Verbal focused attention/concentration: the time taken and the number of errors made on trials 1 to 4 of the Stroop Colour-Word Interference Test; the raw scores on trials A1 and B1 of the Rey Auditory Verbal Learning Test (RAVLT); and the raw score on the Wechsler Intelligence Scale for Children - Revised (WISC-R) Digit Span Forward subtest.
- Verbal divided attention: the raw score on the WISC-R Digit Span Backward subtest.
- Visual focused attention/concentration: the time taken and the number of errors made on the Trail Making Test Part A; the raw score on the WISC-R Picture Completion subtest; the raw score on the WISC-R Coding subtest; and the number of failures to maintain set on the Wisconsin Card Sorting Test (WCST).
- Visual divided attention: the time taken and the number of errors made on the Trail Making Test Part B.

8.2.3 Extraneous Variables

8.2.3.1 Variables That Were Controlled:

1. Race: only Black participants were part of the sample. Adolescents from other race groups were excluded from the sample;
2. Low socio-economic status: operationalised by the area in which the participants live, the number of rooms in their residences, access to water and electricity etc. (see *Appendix 1. Biographical Information Questionnaire)*. This was controlled through sampling;
3. Level of education: participants must have completed at least four years of English medium schooling. Adolescents with less than four years of English medium schooling were excluded from the sample;
4. Language: participants were bilingual, with a functional use of English with at least four years of schooling in the English medium. This was controlled through sampling; and
5. Fatigue of the participants: fatigue is known to negatively affect test performance (Fry, Greenop, & Schutte, 2010). The participants were exposed to either the Neuropsychological Battery or the WISC-R battery first, so as to minimise the effects of fatigue on specific tests that would have been conducted last had the order of tests remained standard. This may have assisted in reducing the confounding effects of fatigue on the tests within this study.

8.2.3.2 Variables That Were Not Controlled:

1. The testing environment: it was not possible to standardise the testing environment. In both the Rahima Moosa Mother and Child Hospital and the Sowetan school, testing took place wherever chairs and tables could be obtained. The researchers tried to guarantee a well-lit and private space, minimising distractions as far as possible, but the conditions were not homogeneous between participants or between the HIV-negative and HIV-positive samples. This could have a potential effect on the reliability and validity of the participants' results (American Psychological Association; APA, 1999);
2. Medical history: it was impossible to control how frequently participants became sick, as well as the presence of any concomitant illnesses at the time that testing took place. These factors could affect cognitive functioning both directly and indirectly. Poorer health, especially diseases of the brain, is associated with reduced cognitive abilities and poorer test performance overall (American Academy of Neurology, 1996);
3. Drug regimen: the drug regimen for each HIV-positive participant was not necessarily homogeneous. ARV regimens with good central nervous system (CNS) penetration, as assessed by central nervous system penetration-effectiveness (CPE) rank, are more effective in controlling cerebrospinal fluid (CSF), and CNS viral replication than regimens with poorer penetration. In a study, Marra et al. (2009) reported that ARVs with good CNS penetration were associated with poorer neurocognitive performance, but recommended that a larger, controlled trial be conducted

before any conclusions regarding the influence of specific ARVs on neurocognitive performance be made;

4. $CD4^+$ count: this relates to the overall health of the individuals. Poor health is generally associated with poor test performance overall (American Academy of Neurology, 1996);
5. Gender: both males and females were included. Males have shown higher Wechsler Adult Intelligence Scale - Revised (WAIS-R) Information subtest scores and faster Finger Tapping scores when compared to females (Saykin et al., 1995). Thus, the genders do not necessarily perform equivalently on neuropsychological tests;
6. Personality: personality traits may be considered to be potential confounders even if traditional matching by demographic criteria has been successfully implemented (Persson, Osterberg, Karlson, & Orbaek, 2000);
7. Motivation: a person with high motivation to do well on the tests may generally result in a better test performance than someone who is not motivated and does not make sufficient effort on the tests. Bailey, Echemendia, and Arnett (2006) found evidence of the negative impact on neuropsychological measures of reduced motivation on test performance;
8. Mood: depression and apathy, as well as other affective disorders, affect neuropsychological test performance (Paradiso, Hermann, Blumer, Davies, & Robinson, 2001);
9. The subjectivity of the researchers: this could have affected the administration of the tests, particularly as a result of variability on rapport and the consequent impact on the assessment; and
10. Possible previous exposure to neuropsychological testing: participants who have been exposed to testing previously are more test wise and have an advantage in test performance compared to others. Performance improvement on repeated neurocognitive tests often occurs because individuals refine their strategies over repeated exposures to a test and, consequently, improve their performance. Practice effects vary as a function of number of administrations, time between administrations, and test complexity (Basso, Bornstein, & Lang, 1999).

8.2.4 Research Design

The researchers had no control over the participants' health or attention and concentration impairment. The investigators are seeking to understand and explain an observed relationship between variables. Thus, this research is a non-experimental, Ex Post Facto, correlational design (Rosnow & Rosenthal, 1996).

8.3 Sample and Sampling

The sample was formed by participants between the ages of 13 years, 0 months and 16 years, 0 months, with at least 4 years of education. The participants had English as, at least, a second language. In this study, it was assumed that because the participants had received at least four years of schooling in the English medium, they were sufficiently fluent and proficient in English for inclusion

in the sample. All participants were of a low socio-economic status, operationalised by the area in which they live, the number of rooms in their residences, access to water and electricity etc. (see *Appendix 1. Biographical Information Questionnaire).* Furthermore, the participants all attended a township-based school and/or a public hospital facility. This assisted in obtaining a more homogeneous group on the basis of socio-economic status. General exclusion criteria from the study included adolescents without a parent or guardian; previous head trauma, neurological or psychiatric conditions; and drug and/or alcohol abuse.

The sample was divided in two groups according to the participants' HIV status. There were 30 HIV-positive adolescents and 71 HIV-negative adolescents. All of the HIV-positive participants were on first-line ARV treatment. The researchers had access to the participants' medical files to confirm the participants' HIV-positive diagnosis and drug regimen. The participants in the HIV-positive sample were sampled through convenience, purposive and snowball sampling methods of patients attending the Rahima Moosa Mother and Child Hospital's Empilweni Clinic, which is an HIV clinic. The HIV-negative participants were selected from a secondary school in the Orlando area of Soweto, South Africa. These participants were sampled through convenience, purposive and snowball sampling methods.

In order to describe the samples, the number of participants and the percentage relative to the sample size, in both the HIV-positive and HIV-negative samples for various descriptors, such as age, gender, current grade, whether a grade had been repeated, and number of years of formal education, are presented in Table 1 below.

Table 1

The Number of Participants in the HIV-Positive and HIV-Negative Samples by Descriptor (Percentages in Brackets)

		Sample Size (*N*)	
Descriptor	Level of Descriptor	HIV-Positive	HIV-Negative
Age	13	9 (30.00)	17 (26.56)
	14	10 (33.33)	20 (31.25)
	15	10 (33.33)	25 (39.06)
	16	1 (3.33)	2 (3.13)
	Missing Data	--	7 (9.86)
Gender	Male	14 (46.67)	33 (50.00)
	Female	16 (53.33)	33 (50.00)
	Missing Data	--	5 (7.04)
Current Grade	7	13 (43.33)	8 (11.43)
	8	8 (26.67)	18 (25.71)
	9	6 (20.00)	42 (60.00)
	10	3 (10.00)	1 (1.43)
	11	0 (0.00)	1 (1.43)
	Missing Data	--	1 (1.43)
Repeated a Grade	Yes	9 (30.00)	15 (21.43)
	No	21 (70.00)	55 (78.57)
	Missing Data	--	1 (1.43)
Years of Formal Education	7	9 (30.00)	3 (4.22)
	8	10 (33.33)	22 (30.99)
	9	5 (16.67)	34 (47.89)
	10	6 (20.00)	10 (14.08)
	11	0 (.00)	1 (1.41)
	Missing Data	--	1 (1.43)

Both the HIV-positive and the HIV-negative sample consisted of participants with a minimum of age of 13 years and a maximum age of 16 years. In the HIV-positive sample, a third of the participants

were 14 years old and another third of the participants were 15 years old. In the HIV-negative sample, almost 40 percent of the HIV-negative participants were 15 years old. The HIV-positive sample comprised 14 males and 16 females; there were marginally more females than males in this sample. The HIV-negative sample comprised 33 males and 33 females; there were equal numbers of males and females in this sample. Most of the participants in the HIV-positive group were in grade 7, whilst most of the participants in the HIV-negative group were in grade 9. Thirty (30) percent of the HIV-positive participants had repeated a grade, in contrast to only 21 percent of the HIV-negative participants having ever repeated a grade. Most of the participants in the HIV-positive sample had received eight years of formal education, whilst most of the participants in the HIV-negative sample had received nine years of formal education.

All of the participants in both samples were Black. This was operationalised because socio-cultural factors, such as socio-economic status, are known to account for significant variations in test performance (Ardila, 1995 as cited in Shuttleworth-Jordan, 1995); by having only Black participants, it was hoped that socio-cultural factors would be mitigated.

8.4 Instruments

8.4.1 Rey Auditory Verbal Learning Test (RAVLT) (Schmidt, 1996; Senior, 2000)

8.4.1.1 Description of the Test

The purpose of the test is to assess verbal learning and memory, including immediate memory span, new learning, susceptibility to interference, and recognition memory. Additionally, overall performance on this measure provides an indication of focused and sustained attention. The RAVLT is a brief, easily administered, measure that utilises pencil and paper. The test has five recall trials followed by a recognition trial. The RAVLT consists of two word lists. The first is a list of 15 nouns, List A. These words are read aloud to the participant, each with a one-second interval between words, for five consecutive trials: these five consecutive trials are referred to as trials A1 – A5 respectively. Each trial is followed by a free recall test. The order of presentation of the words remains fixed across the trials. On completion of Trial A5, an interference list of 15 words, List B, is presented, followed by a free recall test of that list: this trial is referred to as trial B1. Immediately following this, List A is tested without repetition of the words: this is referred to as trial A6. After a 20-minute delay period, the examinee is again requested to recall the words from List A: this is referred to as trial A7. Recognition is then tested: the individual must identify List A words from a list of words containing all items from Lists A and B as well as words that are not part of either list but that are phonemically or semantically similar to those in Lists A and B. Administration time required is 10 - 15 minutes (Strauss, Sherman, & Spreen, 2006).

Forrester and Geffen (1991) assessed 80 Australian children, aged 7 to 15 years on the RAVLT. Van den Burg and Kingma (1999) tested 225 Dutch children, aged 6 to 12 years old. These studies yielded similar results, suggesting that the ability to memorise common, concrete nouns, as tapped by the RAVLT, develops at a similar rate during childhood in Western countries. Furthermore, this has been shown separately for males and females (Vakil, Blachstein, & Sheinmann, 1998).

The total number of words correctly recalled on trials A1 and B1 (Senior, 2000) are indicators of verbal focused and sustained attention/concentration and were thus, used for analysis.

8.4.1.2 Psychometric Information

Internal reliability (coefficient alpha) of the total score is high (about .90; van den Burg & Kingma, 1999). Over one-year intervals, the test has adequate test-retest reliability. Trial A5 and the delayed recall trials were amongst the more reliable scores with *r* values of approximately .60 to .70 (Mitrushina & Satz, 1991).

Delayed recall scores correlate highly with total score ($r > .75$; van den Burg & Kingma, 1999). Percent recall from primacy, middle and recency regions have significant correlations ($r > .80$) with the total number of words recalled. The implication is that they are not pure measures of the traits they reportedly assess (Schmidt, 1997). Correlations between the temporal order of words recalled and various RAVLT scores are weak to high: learning rate, .12; proactive interference, .10; total words, .54; and delayed recall, .64. The strongest relations are with indices that represent the total number of words learned and delayed recall (Vakil & Blachstein, 1994).

In children, reliabilities appear similar to those noted in adults. A sample of 225 children was tested twice, with a three month interval between test sessions, and with alternate versions being given at each testing session. There were no practice effects on the different versions. The most reliable measures were the total number of words recalled ($r = .70$), followed by the 20-minute delayed recall score ($r = .62$) and Trial 5 ($r = .61$). The authors felt that fluctuations in attention explained some of the modest test-retest reliabilities (van den Burg & Kingma, 1999).

The RAVLT correlates moderately well with other measures of learning and memory, such as the Wechsler Memory Scale - Revised (WMS-R; Wechsler, 1987) Logical Memory and Visual Reproduction subtests (Johnstone, Veith, Johnson, & Shaw, 2000) and the California Verbal Learning Test (CVLT; Crossen & Wiens, 1994). Slightly lower scores are obtained on the RAVLT than on the CVLT. The RAVLT may be somewhat harder than the CVLT, requiring more effortful strategies for encoding and retrieval. Specifically, the RAVLT words do not show clear semantic relations, as is the case with the CVLT, and temporal tagging may become a more important strategy (Vakil &

Blachstein, 1994). Factor analytic studies indicate that the RAVLT loads primarily with other verbal memory tests, such as those found on the Wechsler Memory Scale (Johnstone et al., 2000). However, the RAVLT may measure a construct that is not singularly verbal in nature. Factor analyses of variable sets that include the RAVLT indicate that memory variables load together regardless of whether they are verbal or visual (Malec, Ivnik, & Hinkeldy, 1991).

Amongst Black participants, lower levels of acculturation to a Westernised society are linked to lower scores. However, the RAVLT has a long history in the field of psychological assessment and was one of the first standardised tests of multi-trial list learning to achieve widespread use (Kennepohl, Shore, Nabors, & Hanks, 2004).

8.4.2 The Wisconsin Card Sorting Test (WCST) (Heaton et al., 1993; Milner, 1963)

8.4.2.1 Description of the Test

In the WCST, participants are required to discover the rules governing how cards that hold geometrical figures should be sorted. In this task, sorting rules are based on one of the following contingencies: the colour, the shape or the number of figures on each of the cards. In the WCST, such exploration is followed by feedback after each trial (the examiner says "correct" when the sort was correct and "incorrect" when the sort was incorrect). Once participants have discovered the currently active sorting rule, which in the WCST is operationalised as ten correct consecutive responses, the rules by which the cards match change without notice. The participants are then required to use subsequent feedback to observe that the sorting rule has changed and they must discover the new sorting rule (van der Linden, Frese, & Meijman, 2003).

A manual version of the WCST was used. The WCST ended when all 128 cards had been played, or when 6 correct sorts had been achieved (Milner, 1963).

Paniak, Miller, Murphy, Patterson, and Keizer (1996) assessed 685 children aged 9 to 14 years old. The children showed general improvement with increasing age, but did not reach adult performance levels, suggesting that the WCST is sensitive to age-related developing executive functions. For children aged 5 to 8 years, the data collected in Columbia by Rosselli and Ardila (1993) on Spanish-speaking children showed that there were no socio-economic differences.

Difficulties in holding the current sorting rule active in mind, and/or lapses in task set maintenance are often due to a lapse in attention or concentration (Hartman, Bolton, & Fehnle, 2001). Thus, the number of failures to maintain set on the WCST (Heaton et al., 1993) was used as a measure of visual sustained attention/concentration.

8.4.2.2 Psychometric Information

The WCST has been proven to be an exceptionally good test at identifying frontal lobe abnormalities, with a reliability of .84. Heaton et al. (1993) report test-retest reliabilities ranging from .37 to .72 in children and adolescents on perseverative and non-perseverative errors respectively. The WCST has been shown to have modest correlations with measures of attention, including continuous performance tasks and the Trail Making Test Part B (Strauss, Sherman, & Spreen, 2006).

Test results for Hispanic groups appear equivalent to those obtained with English-speaking individuals. Strauss, Sherman and Spreen (2006) hold that socio-economic conditions affect performance on this test; by implication, low socio-economic groups in South Africa would be disadvantaged compared to higher socio-economic groups. Educational level shows only modest correlations with WCST scores. A study was conducted by Tsuchiya, Oki, Yahara, and Fujieda (2005), which showed no significant differences in results for the variables age, gender, number of categories achieved, or number of errors made on the WCST. Previous research has demonstrated that education affects performance on the WCST only to a small degree. Gender has been shown to affect performance on the WCST, but this finding was not significant prior to the age of 45 (Strauss, Sherman, & Spreen, 2006).

8.4.3 Stroop Colour-Word Interference Test (Golden, 1978; Moering et al., 2003)

8.4.3.1 Description of the Test

The Stroop Colour-Word Interference Test is a measure of cognitive flexibility and executive function, as well as a measure of focused attention. There are four parts to the test. In Part 1, the subject names the colour of rectangular blocks printed in coloured ink (blue, green, red or yellow). In Part 2, the subject reads randomised colour names (blue, green, red or yellow) printed in black ink. In Part 3, the subject has to name the colour of the ink (blue, green, red or yellow) and not read the actual word. In Part 4, for words that are not printed in the rectangular squares, the subject has to name the colour of the ink (blue, green, red or yellow) and not read the actual word; but for words that are printed in the rectangular squares, the subject has to read the word and disregard the colour used to print the word. There are 50 items in each part of the test (Golden, 1978; Moering et al., 2003).

Age has been shown to have a significant impact on the interference score on the Stroop Colour-Word Interference Test in adults (r = .41; Troyer, Leach, & Strauss, in press), especially on the interference trial. This correlation was r = .29 in children (Golden & Golden, 2002).

The time taken on trials 1 to 4 of the Stroop Colour-Word Interference Test (Golden, 1978; Moering et al., 2003) is a measure of focused attention/concentration. Furthermore, the number of errors made,

including uncorrected and self-corrected errors, due to lapses in concentration, on the four trials is an indicator of verbal focused attention/concentration.

8.4.3.2 Psychometric information

The test-retest reliability for the Stroop Colour-Word Interference Test is high with the word item coefficient at .83, the colour coefficient at .74, and the colour-word coefficient at .67 (van der Elst, van Boxtel, van Breukelen, & Jolles, 2006). Lezak (1995) maintains that the Stroop Colour-Word Interference Test is reliable. Golden (1978) reports reliabilities of .89 for the word trial, .84 for the colour trial, and .73 for the colour-word trial (n = 450).

Bullock et al. (unpublished data, as cited in Strauss, Sherman, & Spreen, 2006) examined young adults on the Stroop Colour-Word Interference Test, with a one-month interval between test sessions. Reliability coefficients were high: coefficients of .90, .83, and .91 were found for the first three trials of the test. However, the participants were noted to show significant practice effects, with performance improving by 2 to 5 seconds on the second administration,

Correlations amongst test trials tend to be moderate/high, suggesting they are tapping similar abilities (Chafetz, & Matthews, 2004). The interference scores correlate moderately well with other measures of attention, including omission errors on continuous performance tasks (Strauss, Sherman, & Spreen, 2006). The interference score is moderately related to the difference score between the Trail Making Test Parts A and B (.55; May & Hasher, 1998).

Ethnicity impacts test scores, with Black participants performing at a lower level than Caucasians. Performance also tends to be slower in bilinguals. Thus, caution should be applied when interpreting the scores (Strauss, Sherman, & Spreen, 2006).

8.4.4 <u>The Trail Making Test (Army Individual Test Battery, 1944)</u>

8.4.4.1 Description of the Test

The test requires the subject to connect 25 encircled numbers that are randomly arranged on a page by making pencil lines, in the correct order (Part A), and 25 encircled numbers and letters that are randomly arranged on a page in alternating order (Part B). The standard procedure includes practice exercises for Parts A and B (Strauss, Sherman, & Spreen, 2006).

The time taken, as well as the number of errors made, on the Trail Making Test Part A (Army Individual Test Battery, 1944) was used as a measure of visual focused attention/concentration.

The time taken, as well as the number of errors made, on the Trail Making Test Part B (Army Individual Test Battery, 1944) was used as a measure of visual divided attention.

8.4.4.2 Psychometric Information

The Trail Making Test has been found to be of adequate reliability in children from 9 to 14 years; test-retest reliability was .41 on Part A and .65 on Part B (Barr, 2003). In young adults retested after an interval of 3 weeks, reliability was low for Part A (.55) but adequate for Part B (.75; Bornstein, Baker, & Douglas, 1987). Over short retest intervals, practice effects emerge. Bornstein et al. (1987) retested a sample of healthy adults after a three-week interval and noted significant improvements (about three seconds) for Part A. Inter-rater reliability has been reported as .94 for Part A and .90 for Part B (Fals-Stewart, 1991).

Part A and Part B correlate moderately well with each other (.60), suggesting that they measure similar functions (Heilbronner, Henry, Buck, Adams, & Fogle, 1991). The Trail Making Test has been found to correlate with other tests of attentional abilities, including the Visual Search and Attention Test, and the Paced Serial Attention Test (Royen, Tombaugh, Rees, & Francis, 2004).

Cultural variables may affect performance on the Trail Making Test; Black unacculturated participants may take longer to complete it. As the participants in this study all reside in urban Johannesburg and attend a Westernised schooling system, this may be taken to assist in mitigating this factor. However, monolinguals have been found to perform faster than bilinguals. Thus, caution should be applied when interpreting the scores (Strauss, Sherman, & Spreen, 2006).

8.4.5 Wechsler Intelligence Scale for Children - Revised (WISC-R) (Wechsler, 1974) Subtests

The use of the WISC-R over the more modern Wechsler Intelligence Scale for Children – Third Edition (WISC-III) or the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV) was decided upon for resource-constraint reasons.

8.4.5.1 The Coding subtest of the Wechsler Intelligence Scale for Children - Revised (WISC-R) (Wechsler, 1974)

8.4.5.1.1 Description of the Test

Making use of a key, the subject is required to copy symbols that are randomly paired with numbers (from one to nine) within a specified time limit. A practice trial is administered; the subject must fill in the blank spaces with the symbol that is paired to the number above the blank space. The test itself is then administered and the examinee is given 120 seconds to complete as many of the symbols as possible. Subjects are encouraged to complete the task as quickly and accurately as possible, but they are not told beforehand of the length of time they will be allowed to complete the task (Lezak, 1995).

The raw score on the Coding subtest of the WISC-R (Wechsler, 1974) was used as a measure of visual sustained attention/concentration.

8.4.5.1.2 Psychometric Information

Test-retest reliability tends to run high, with correlations in the .82 to .88 range (Wechsler, 1981). Reports of practice effect sizes are modest, but a small sample of adults in their 30s showed a 7 percent gain on retest following a 15-month interval (Miller et al., 1984). Correlations with Wechsler Adult Intelligence Scale – Revised (WAIS-R) tests ranged from .21 to .44 (Wechsler, 1981), suggesting that mental ability does not contribute greatly to success on this test.

8.4.5.2 The Digit Span subtest of the Wechsler Intelligence Scale for Children - Revised (WISC-R) (Wechsler, 1974)

8.4.5.2.1 Description of the Test

The WISC-R Digit Span subtest comprises two parts, the Digit Span Forward and the Digit Span Backward, which are administered separately. Both tests consist of seven pairs of random number sequences that the examiner reads aloud at the rate of one per second. The examinee is then required to repeat the digits to the examiner in exactly the same order (the Digit Span Forward) or in reverse order (the Digit Span Backward). When a sequence is repeated correctly, the examiner reads the next, longer number sequence. This continues until the examinee fails a pair of sequences or repeats the longest series correctly (Wechsler, 1974).

The number of items correctly reproduced on the WISC-R Digit Span Forward subtest (Wechsler, 1974) was used as a measure of verbal focused attention/concentration.

The number of items correctly reproduced on the WISC-R Digit Span Backward subtest (Wechsler, 1974) was used as a measure of verbal divided attention.

8.4.5.2.2 Psychometric Information

What the Digit Span Forward subtest measures is more closely related to the efficiency of attention, or freedom from distractibility, than to memory. Practice effects are negligible (McCaffrey, Duff, & Westervelt, 2000). Test-retest reliability coefficients range from .66 to .89 (Matarazzo & Herman, 1984). The magnitude of internal reliability coefficients for the Digit Span test for the standardisation sample was high (in the .80 to .89 range). The test-retest reliability coefficients for the standardisation sample were also high, in the .80 to .89 range (Wechsler, 2003)

8.4.5.3 The Picture Completion subtest of the Wechsler Intelligence Scale for Children - Revised (WISC-R) (Wechsler, 1974)

8.4.5.3.1 Description of the Test

During administration of the WISC-R Picture Completion subtest the examiner shows the subject incomplete colour pictures of human features, familiar objects, or scenes, arranged in order of difficulty, with instructions to point out what important part is missing (Wechsler, 1974).

The raw score on the WISC-R Picture Completion subtest (Wechsler, 1974) was used as a measure of visual focused attention/concentration.

8.4.5.3.2 Psychometric Information

White participants tend to outperform African-American participants by about two points on average throughout the WISC-R age ranges (Kaufman, McLean, & Reynolds, 1988). Split-half reliability for the normative population was .82 (Wechsler, 1981). Test-retest reliability coefficients for the normative population were .86 and .89. The average test-retest gain, with an interval of 1 year, was 1.1 scaled score point (Matarazzo & Herman, 1984). Retesting a subset of the normative sample an average of 35 days later produced a 2.4 scaled score point gain.

The WISC-R Picture Completion subtest correlates higher (.67) with the WISC-R Information subtest than any other subtest except the WISC-R Comprehension subtest, thus reflecting the extent to which it also tests remote memory and general information (Lezak, 1995).

8.5 Procedure

8.5.1 Pre-Experimental

1. Ethics was obtained from formal structures within the University of the Witwatersrand (see *Appendix 2: Human Research Ethics Committee (Medical) Approval*).
2. Permission for testing the HIV-positive group was obtained from the Empilweni Clinic at the Rahima Moosa Mother and Child Hospital (see *Appendix 3: Consent Form from the Empilweni Clinic at the Rahima Moosa Mother and Child Hospital*).
3. Permission for testing the HIV-positive group using the Psychiatry/Psychology Department offices at Rahima Moosa Mother and Child Hospital was obtained (see *Appendix 4: Permission from the Rahima Moosa Mother and Child Hospital Psychiatry/Psychology Department*).
4. Permission for testing the HIV-negative group was obtained from the Department of Education (see *Appendix 5: Gauteng Department of Education Research Approval Letter*) and the Sowetan school itself.
5. The researchers approached the Rahima Moosa Mother and Child Hospital, as well as the school in Soweto, and explained the research to the relevant person(s) in charge.

6. For the HIV-negative sample, a letter was sent home with the adolescents from school explaining the purpose and requirements of the research (see *Appendix 6: Parental Information Sheet {Contrast group}*). The letter requested that the parents and/or guardians of the adolescents read and sign the letter giving permission for their child to participate in the study (see *Appendix 7: Parental Consent Form {Contrast Group}).*
7. For the HIV-positive sample, participants and their parents and/or guardians were approached at the Rahima Moosa Mother and Child Hospital and asked to participate in the research.
8. The participants who agreed to take part in the study were required to sign assent forms (see *Appendix 8: Participant Assent Form {Experimental Group})*. Their parents and/or guardians were required to sign consent forms (see *Appendix 9: Parental Consent Form {Experimental Group}).*

8.5.2 Experimental

8.5.2.1 Procedure for the HIV-Positive Sample

Data gathering for the HIV-positive sample took place at the Rahima Moosa Mother and Child Hospital. The researchers had access to the patient files and, based on the information contained therein, completed a Participant Selection Form (see *Appendix 10: Participant Selection Form*). Patients attending the Rahima Moosa Mother and Child Hospital for their clinical check-ups who met the inclusion criteria were approached and invited to participate in the study.

Where possible, a neutral party, such as an employee at the Rahima Moosa Mother and Child Hospital, invited the adolescent and their guardian to participate in the study whilst they waited for their check-up. This was implemented, as far as possible, to ensure that the patients and their guardians felt that they could decline to be part of the research without any fear of negative consequences. Where a neutral party was not available, the researchers themselves approached the potential participants and their guardians regarding the possibility of participating in the study, whilst emphasising that they could decline to participate without fear of negative consequences. Consenting participants were taken for testing directly after their regular clinical check-up, or they were brought back to the clinic during the testing process for their check-up to take place. In this instance, the testing was completed on conclusion of the clinical check-up. It was ensured, as far as possible, that the testing protocol did not interfere with the medical interventions in any way.

The participants and their parents and/or guardians were each given an information letter (see *Appendix 11: Parental Information Sheet {Experimental group}* and *Appendix 12: Participant Information Sheet {Experimental Group});* and either a consent or an assent form (see *Appendix 9: Parental Consent Form {Experimental Group}* and *Appendix 8: Participant Assent Form*

{Experimental group}) prior to the administration of the test battery. Prospective participants had the process of the research explained to them and then they were asked to complete an assent form. Their legal guardian was asked to fill in a consent form. Where the guardian was not either literate or proficient in the English language, a medical professional at the Rahima Moosa Mother and Child Hospital or the prospective research subject (who attends school in the English medium) assisted with translation.

The battery of tests was administered to the participants individually, by one of the researchers. There were seven testers who were involved in the administration of the battery for the HIV-positive sample. The testers included six Masters students in the MA(Neuropsychology) degree, and one Masters student in the MA(Psychology) degree. Quiet venues for the testing process were organised within the Psychiatry/Psychology department of the hospital, as well as near the Empilweni Clinic.

On average, the test battery took between four and five hours to complete. The participants were required to set aside this amount of time for testing.

In the testing session, the following tests were run:

1. Biographical Questionnaire (see *Appendix 1. Biographical Information Questionnaire)*; and
2. Becks Youth Inventory.

8.5.2.1.1 The Neuropsychological Battery:

1. Finger Tapping Test;
2. Grooved Pegboard Test;
3. Rey Osterreith Complex Figure Test (ROCFT) Copy Trial;
4. ROCFT Immediate Recall Trial;
5. RAVLT Immediate Recall Trials;
6. Trail Making Test;
7. ROCFT Delayed Recall Trial;
8. ROCFT Delayed Recognition Trial;
9. RAVLT Delayed Recall Trial;
10. RAVLT Delayed Recognition Trial;
11. Controlled Oral Word Association Test;
12. Stroop Colour-Word Interference Test;
13. WCST;
14. A fifteen minute break after approximately two hours of testing.

8.5.2.1.2 WISC-R subtests:

1. Information;
2. Picture Completion;
3. Similarities;
4. Picture Arrangement;
5. Arithmetic;
6. Block Design;
7. Vocabulary;
8. Object Assembly;
9. Comprehension;
10. Mazes;
11. Coding; and
12. Digit Span.[1]

A light lunch was provided for the participants during the fifteen minute break.

The participants were exposed to either the Neuropsychological Battery or the WISC-R subtests first, in order to minimise the effects of fatigue on specific tests that would have been conducted last had the order of tests remained the same across every participant. As far as possible, alternate participants were exposed to the reversed battery. The participants remained with the same researcher for the duration of the battery, but the researcher administered the two halves of the battery in the relevant order.

Once the participants had completed the test battery, they were given transport reimbursement money and they were required to sign a letter stating that they had received the reimbursement (see *Appendix 13: Reimbursement Letter*).

8.5.2.2 Procedure for the HIV-Negative Sample

Data gathering for the HIV-negative sample took place at a secondary school in Soweto. The teachers at the school, who were aware of the students' HIV status, selected suitable candidates to participate in the study, based on the inclusion criteria that had been provided to them in advance. The teachers arranged for the students, should they have assented and their parents and/or guardians have consented, to be at the school during the school holidays for testing to take place: the contrast group participants were tested with as little disruption to the school timetable as possible.

[1] A variety of tests, and not only the tests that were specifically required for the current research study, were administered to the participants. These other tests were required for the overall research project, and for the other researchers' studies.

The teachers sent the various letters and forms home with the relevant adolescents. Thus, the participants and their parents and/or guardians were each given an information letter (see *Appendix 6: Parental Information Sheet {Contrast group}* and *Appendix 14: Participant Information Sheet {Contrast Group}*) and either a consent or an assent form (see *Appendix 7: Parental Consent Form {Contrast Group}* and *Appendix 15: Participant Assent Form {Contrast group})* prior to the administration of the test battery. All of the relevant forms were required to be signed prior to testing. Where the legal guardian was not either literate or proficient in the English language, a staff member of the school or the prospective research subject (who attends school in the English medium) assisted with translation. Participants had the process of the research explained to them again on the day of testing by the research team, and some members of the school staff were present to oversee the proceedings.

The battery of tests was administered to the participants individually, by different researchers at the school in Soweto. The testers included six Masters students in the MA(Neuropsychology) degree, one Masters student in the MA(Psychology) degree, two Honours students in the BA Hons(Psychology) degree, one psychometric intern and two First Year students in the BA(Psychology) degree. Venues for the testing process were organised at the school; testing took place one-on-one but in a group setting, either in the school hall or in the quadrangle which was outside the school hall.

On average, the neuropsychological test battery took between four and five hours to complete. The participants were required to set aside this amount of time for testing. In the testing session, the same tests were run as were for the HIV-positive sample. Again, a light lunch was provided for the participants during the fifteen minute break.

Once the participants had completed the test battery, they were given transport reimbursement money and they were required to sign a letter stating that they had received the reimbursement (see *Appendix 13: Reimbursement Letter*).

8.6 Ethical Considerations

Ethical clearance was first granted from formal structures within the University of the Witwatersrand.

Permission for testing the HIV-positive group was obtained from the Empilweni Clinic. Permission for testing the HIV-negative group was obtained from the Department of Education and from the Sowetan secondary school itself.

Participants were above the age of assent, but not above the age of consent. The researchers, or acceptable other individuals, explained the research to the participants and their parents and/or

guardians, and the participants were then invited to be involved in the study. Participants were each required to fill in an assent form and their legal guardians were each required to fill in a consent form.

The children in the HIV-positive sample all attend the Empilweni HIV clinic and are on ARVs. Considering this, each participant should have been aware of their HIV status. Nevertheless, due to the sensitive nature of an HIV-positive diagnosis, the participants in this sample were informed that the research aimed to investigate the effects of the treatment they were receiving; and the effects of HIV itself were not elaborated upon.

Confidentiality was guaranteed. However, as the participants needed to be present for the testing, anonymity was impossible. If any participant, for any reason, experienced distress, they were provided with the contact details of free counselling services and/or they were allowed to discontinue testing.

All of the tests that were performed were non-invasive, manual, pencil-and-paper tests and therefore, no harm befell the participants. As the testing process took several hours, lunch and refreshments were provided for the participants and their guardians (if present).

Participants in the HIV-negative sample were asked to attend testing sessions during the school holidays so that no school was missed.

The participants that travelled to the school and/or the Rahima Moosa Mother and Child Hospital for the purpose of testing had their travelling costs reimbursed. The participants were required to sign reimbursement letters (see *Appendix 13: Reimbursement Letter*) confirming that the payment had been received.

9. Results

In terms of the structure of the results section, the means, standard deviations, minima and maxima for the various clinical data of the Human Immunodeficiency Virus (HIV)-positive participants, including the age at which Highly Active Anti-Retroviral Therapy (HAART) was commenced, the duration of anti-retroviral (ARV) treatment, the World Health Organisation (WHO) stage at diagnosis, the starting and current $CD4^+$ counts, and the starting and current viral loads, are presented first. Thereafter, descriptive statistics including the means, standard deviations, minima and maxima for the HIV-positive participants for each of the dependent variables, as operationalised by performance on the neuropsychological tests, are provided.

Following this, the comparability of the HIV-positive and HIV-negative samples in terms of age and the number of years of formal education is addressed using Student's t-Tests. The issue of the normality of the raw data is then examined through the use of the Kolmogorov-Smirnov Test, informing whether parametric or non-parametric tests are appropriate.

Subsequently, the dependent variables are used as a structure for the presentation of the main findings of this research. Where the requirements of normality of the data were met, Student's t-Tests and F Tests were run to compare the HIV-positive and the HIV-negative participants' performance on the neuropsychological tests. Where the requirements of normality of the data were not met, Mann-Whitney U Tests were run to compare the HIV-positive and the HIV-negative participants' performance on the neuropsychological tests. Then, comparisons between the dependent variables are provided using Pearson's Product-Moment Correlations where the data was normally distributed and Spearman's Rank-Order Correlations where the data was not normally distributed.

Lastly, the results section goes on to examine the impact of the various clinical variables of the HIV-positive participants on the neuropsychological test results. These include the age at which HAART was commenced, the duration of ARV treatment, the WHO stage at diagnosis, the starting and current $CD4^+$ counts, and the starting and current viral loads.

Importantly, all data that was available for analysis was included; outliers were included in the analyses.

9.1 Descriptions

9.1.1 Description of the Clinical Information of the HIV-Positive Group

Within the HIV-positive group, clinical variations were considered, such as:

1. The age at which HAART was commenced;
2. The duration of ARV treatment;
3. The WHO stage at diagnosis;
4. The starting and current $CD4^+$ counts; and
5. The starting and current viral loads.

None of these variations applied to the HIV-negative participants. The results are shown below in Table 2.

Table 2

A Summary of the Clinical Information of the HIV-Positive Participants

Clinical Information of the HIV-Positive Group	Mean Values (Standard Deviation, Minimum and Maximum in Brackets)
Age at which HAART was commenced (Years)	7.93 (3.00; 1; 13)
Number of Years on HAART	6.15 (3.04; 1; 14)
WHO Stage at Diagnosis (Stages 1-4)	3.07 (1.52; 1; 4)
$CD4^+$ Count when HAART was commenced	564.07 (1,106.91; 16; 6,239)
Current $CD4^+$ Count	625.82 (268.83; 21; 1,014)
Viral Load when HAART was commenced	222,656.23 (305,965.00; 25; 1,100,000)
Current Viral Load	16,620.68 (53,014.30; 25; 240,000)

As shown in the table above, the mean age at which HAART was commenced was 7.93 years with a standard deviation of 3.00. The range of ages at which HAART was commenced is very wide, indicating that the participants have been using ARVs for widely disparate time periods. Furthermore,

the mean duration of ARV treatment was 6.15 years with a standard deviation of 3.04. Thus, most of the participants had been on ARVs for one-third to half of their life span.

The mean WHO stage at diagnosis was 3.07 with a standard deviation of 1.52. This indicates that most of the participants were in WHO stage 3 at the time of diagnosis and were thus, symptomatic.

The mean starting $CD4^+$ count was 564.07 with a standard deviation of 1,106.91. Thus, most of the participants were at the low end of the normal range regarding their $CD4^+$ cell counts when they were started on ARV treatment. The mean current $CD4^+$ count was 625.82 with a standard deviation of 268.83, indicating that most participants have benefited from being on ARV treatment and their $CD4^+$ count had increased.

The mean starting viral load was 222,656.23 with a standard deviation of 305,965.00, and the mean current viral load was 16,620.68 with a standard deviation of 53,014.30, again indicating that most participants have benefited from being on ARV treatment and their viral load had decreased.

9.1.2 Description of the Neuropsychological Test Performance of the HIV-Positive Group

Means ($\bar{x}$), standard deviations (*SD*), minima, maxima and medians were calculated for the HIV-positive group for each of the neuropsychological tests. Only the HIV-positive sample is described below, as the HIV-negative group was used solely for comparison purposes. The results are shown below in Table 3.

Table 3

A Summary of the Means of the Neuropsychological Test Results of the HIV-Positive Participants (Standard Deviation; Minimum; Maximum; and Median in Brackets)

Test	Test Component	HIV-Positive Group Means (N = 30)
RAVLT	Total number of words correctly recalled on trial A1	5.87 (1.85; 2; 10; 6)
	Total number of words correctly recalled on trial B1	5.30 (1.90; 2; 9; 5)
WCST	Number of failures to maintain set	.67 (.96; 0; 4; 0)
Stroop Colour-Word Interference Test	Time taken on trial 1	51.27 (10.48; 33; 77; 49)
	Number of uncorrected errors made on trial 1	1.17 (1.41; 0; 5; 1)
	Number of self-corrected errors made on trial 1	2.07 (1.64; 0; 6; 2)
	Time taken on trial 2	38.77 (11.97; 24; 70; 37)
	Number of uncorrected errors made on trial 2	.40 (.72; 0; 2; 0)
	Number of self-corrected errors made on trial 2	1.37 (1.38; 0; 5; 1)
	Time taken on trial 3	95.23 (4.30; 50; 140; 94)
	Number of uncorrected errors made on trial 3	4.20 (4.16; 0; 17; 3)
	Number of self-corrected errors made on trial 3	4.20 (3.08; 0; 12; 3.5)

Table 3

A Summary of the Means of the Neuropsychological Test Results of the HIV-Positive Participants (Standard Deviation; Minimum; Maximum; and Median in Brackets)…Continuation Part A

Test	Test Component	HIV-Positive Group Means (N = 30)
Stroop Colour-Word Interference Test	Time taken on trial 4	99.03 (24.00; 50; 148; 102)
	Number of uncorrected errors made on trial 4	5.60 (4.16; 0; 16; 5)
	Number of self-corrected errors made on trial 4	3.27 (2.57; 0; 9; 2.5)
Trail Making Test	Time taken on Part A	65.53 (22.43; 36; 118; 59.5)
	Number of errors made on Part A	.43 (.73; 0; 3; 0)
	Time taken on Part B	149.83 (63.65; 65; 335; 129)
	Number of errors made on Part B	2.53 (3.59; 0; 15; 1)
WISC-R Coding Subtest	Raw Score	39.45 (10.29; 21; 57; 38)
WISC-R Picture Completion Subtest	Raw Score	15.63 (3.99; 9; 24; 17)
WISC-R Digit Span Subtest	Number of items correctly reproduced on the Digit Span Forward	5.00 (1.65; 2; 10; 5)
	Number of items correctly reproduced on the Digit Span Backward	3.17 (1.39; 1; 6; 3)

As can be seen from the table above, the HIV-positive participants were able to recall a slightly higher number of words on trial A1 than on trial B1 of the Rey Auditory Verbal Learning Test (RAVLT).

On average, the HIV-positive participants made less than one failure to maintain set on the Wisconsin Card Sorting Test (WCST).

The HIV-positive participants were able to complete trial 2 of the Stroop Colour-Word Interference Test quicker than any of the other trials, whilst they took the longest time to complete trial 4. They made the fewest number of uncorrected errors on trial 2, whilst they made the highest number of uncorrected errors on trial 4. The HIV-positive participants made the fewest number of self-corrected errors on trial 2, whilst they made the highest number of self-corrected errors on trial 4 of the Stroop Colour-Word Interference Test.

The HIV-positive participants completed the Trail Making Test Part A quicker and made fewer errors than on the Trail Making Test Part B.

The range of the raw scores on the Wechsler Intelligence Scale for Children – Revised (WISC-R) Coding subtest was wide, whilst the range of the raw scores on the WISC-R Picture Completion subtest was narrower.

The HIV-positive participants were able to reproduce slightly longer strings of digits on the Digit Span Forward phase than on the Digit Span Backward phase of the WISC-R Digit Span Subtest.

9.2 Comparisons

9.2.1 Normality of the Data

Before comparing the HIV-positive and the HIV-negative groups or conducting further analyses, it was important to ascertain the normality of the data. Given the nature of the neuropsychological tests, the data obtained from all the tests was in the form of interval data. The raw data was subjected to Kolmogorov-Smirnov Tests to determine if it was normally distributed. The results are shown below in Table 4.

Table 4

Results of Kolmogorov-Smirnov Tests of Normality

Test	Test Component	Statistic (Kolmogorov-Smirnov = *D*)
RAVLT	Total number of words recalled on trial A1	.15 (<.010)*
	Total number of words recalled on trial B1	.12 (<.010)*
WCST	Number of failures to maintain set	.27 (<.010)*
Stroop Colour-Word Interference Test	Time taken on trial 1	.09 (.023)*
	Time taken on trial 2	.18 (<.010)*
	Time taken on trial 3	.09 (.018)*
	Time taken on trial 4	.11 (<.010)*
Trail Making Test	Time taken on Part A	.12 (<.010)*
	Time taken on Part B	.16 (<.010)*
WISC-R Coding Subtest	Raw Score	.08 (.099)
WISC-R Picture Completion Subtest	Raw Score	.16 (<.010)*
WISC-R Digit Span Subtest	Items correctly reproduced on Digits Forward	.18 (<.010)*
	Items correctly reproduced on Digits Backward	.19 (<.010)*

Note. *p < .05

As can be seen from the results, all of the tests, with the exception of the WISC-R Coding Subtest, were not normally distributed. Because this data was not normally distributed, non-parametric tests were deemed appropriate and were run for all of the neuropsychological tests, whilst parametric tests were used for the WISC-R Coding Subtest (Howell, 2004).

9.2.2 Comparisons Indicating the Homogeneity of the Data of the Two Samples

Two-tailed Student's t-Tests were run to ensure that the HIV-positive and the HIV-negative groups were not significantly different from each other with regards to age and education. The results are shown below in Table 5.

Table 5

Results of the Student's t-Test

Variable	Test		Statistic	p-Value	
Age	Student's t	*t*	-.38	Pr > |t|	.70
Years of Education	Student's t	*t*	-1.39	Pr > |t|	.17

Note. *p < .05

As can be seen from the table above, the two groups were not significantly different from each other in terms of age or the number of years of education. Based on this, the two groups were deemed to be homogeneous in terms of age and education.

9.2.3 Comparisons of the Performance on the Neuropsychological Tests of the Two Samples

As previously noted, the general aim of the current research study was the comparison of the attention and concentration functions in adolescents between the ages of 13 and 16 years living with HIV, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, compared to an equivalent contrast group of HIV-negative adolescents. One of the specific aims of the current research study was to identify group differences of attention and concentration functions between adolescents with HIV, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, and a contrast group of HIV-negative adolescents. In order to address these aims, two sample Student's t-Tests were run on the parametric data, comparing the performance of the HIV-positive and the HIV-negative participants on each of the dependent variables, as operationalised as scores on the various neuropsychological tests. Likewise, in order to address the aims, Mann-Whitney U Tests were run on the non-parametric data. The results of these Students t-Tests and Mann-Whitney U (MWU) Tests are outlined in Table 6 below.

Table 6

Results of the Two Sample t-Tests and Mann-Whitney U Tests

Test Component (Mean)	Test	Statistic		p-Value	
Number of words recalled on trial A1 of the RAVLT	MWU	U	938.5	Pr > |U|	.404
Number of words recalled on trial B1 of the RAVLT	MWU	U	570	Pr > |U|	<.0001*
Number of failures to maintain set on the WCST	MWU	U	1130	Pr > |U|	.457
Time taken on trial 1 of the Stroop Colour-Word Interference Test	MWU	U	887.5	Pr > |U|	.008*
Time taken on trial 2 of the Stroop Colour-Word Interference Test	MWU	U	978.5	Pr > |U|	.038
Time taken on trial 3 of the Stroop Colour-Word Interference Test	MWU	U	1015	Pr > |U|	.066
Time taken on trial 4 of the Stroop Colour-Word Interference Test	MWU	U	1022	Pr > |U|	.074
Number of uncorrected errors on trial 1 of the Stroop Colour-Word Interference Test	MWU	U	780.5	Pr > |U|	<.0001*
Number of uncorrected errors on trial 2 of the Stroop Colour-Word Interference Test	MWU	U	974	Pr > |U|	.036*
Number of uncorrected errors on trial 3 of the Stroop Colour-Word Interference Test	MWU	U	776.5	Pr > |U|	<.0001*
Number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test	MWU	U	681.5	Pr > |U|	<.0001*
Number of self-corrected errors on trial 1 of the Stroop Colour-Word Interference Test	MWU	U	642.5	Pr > |U|	<.0001*
Number of self-corrected errors on trial 2 of the Stroop Colour-Word Interference Test	MWU	U	602.5	Pr > |U|	<.0001*
Number of self-corrected errors on trial 3 of the Stroop Colour-Word Interference Test	MWU	U	952.5	Pr > |U|	.025*

Table 6

Results of the Two Sample t-Tests, F Tests and Mann-Whitney U Tests…Continuation Part A

Test Component (Mean)	Test	Statistic		p-Value	
Number of self-corrected errors on trial 4 of the Stroop Colour-Word Interference Test	MWU	U	1049	Pr > |U|	.108
Time taken on Part A of the Trail Making Test	MWU	U	934.5	Pr > |U|	.018*
Number of errors on Part A of the Trail Making Test	MWU	U	901	Pr > |U|	.009*
Time taken on the Trail Making Test Part B	MWU	U	993	Pr > |U|	.05
Number of errors on Part B of the Trail Making Test	MWU	*U*	742.5	Pr > |U|	<.0001*
Raw score on the WISC-R Coding subtest	Student's t	*t*	-2.22	Pr > |U|	.029*
Number of digits recalled on the Digits Forward trial of the WISC-R Digit Span Subtest	MWU	U	1125	Pr > |U|	.429
Number of digits recalled on the Digits Backward trial of the WISC-R Digit Span Subtest	MWU	U	1162	Pr > |U|	.591
Raw score on the WISC-R Picture Completion subtest	MWU	U	937	Pr > |U|	.080

Note. *p < .05

As can be seen from the table above, the mean number of words recalled on trial B1 of the RAVLT; the mean time taken on the Trail Making Test Part A; the mean number of errors on the Trail Making Test Part A and B; the mean raw score on the WISC-R Coding subtest; as well as the mean time taken on trial 1; the mean number of uncorrected errors on trials 1, 2, 3 and 4; and the mean number of self-corrected errors on trials 1, 2 and 3 of the Stroop Colour-Word Interference Test were significantly different between HIV-positive individuals and HIV-negative individuals. The remainder of the comparisons of the neuropsychological tests in the two samples were not significantly different from each other.

9.2.4 Spearman's Rank-Order Correlations between the Two Samples on the Neuropsychological Tests

In order to investigate one of the specific aims of the current research study, that is, to identify group differences of attention and concentration functions between adolescents with HIV, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, and a contrast group of HIV-negative adolescents, Spearman's Rank-Order Correlations were run.

These were run only on the non-normally-distributed data, comparing the results of the HIV-positive and the HIV-negative participants on each of the dependent variables, as operationalised as scores on the various neuropsychological tests. The results of these Spearman's Rank-Order Correlations are outlined in Table 7 below.

Table 7

Results of the Spearman's Rank-Order Correlations of the Various Neuropsychological Tests

Test Comp-onent	A1 RAVLT	B1 RAVLT	Time Trail Making Test A	Errors Trail Making Test A	Time Trail Making Test B	Errors Trail Making Test B	Uncorrec-ted Errors Trial 1 Stroop	Self-corrected Errors Trial 1 Stroop	Time Trial 1 Stroop	Uncorrec-ted Errors Trial 2 Stroop	Self-corrected Errors Trial 2 Stroop	Time Trial 2 Stroop	Uncorrec-ted Errors Trial 3 Stroop	Self-corrected Errors Trial 3 Stroop	Time Trial 3 Stroop	Uncorrec-ted Errors Trial 4 Stroop	Self-corrected Errors Trial 4 Stroop	Time Trial 4 Stroop	WISC-R Picture Complet-ion	WISC-R Digits Forward	WISC-R Digits Backwar d	WCST Failures To Maintain Set
A1 RAVLT	1.000	.364 (<.0001*)	-.241 (-.016*)	-.077 (.449)	-.217 (.030*)	.026 (.798)	.121 (.232)	-.129 (.198)	-.118 (..241)	-.244 (.014*)	.108 (.287)	-.049 (.629)	-.020 (.839)	-.069 (.497)	-.066 (.513)	-.065 (.521)	.041 (.687)	-.067 (.509)	.186 (.068)	.246 (.015*)	.162 (.111)	.033 (.745)
B1 RAVLT	.364 (<.0001*)	1.000	-.569 (<.0001*)	-.115 (.256)	-.554 (.<.0001*)	-.298 (.003*)	-.104 (.304)	-.286 (.004*)	-.573 (<.0001*)	-.128 (.204)	-.236 (.018*)	-.338 (<.0001*)	.082 (.416)	-.059 (.561)	-.333 (<.0001*)	-.253 (.011*)	.050 (.621)	-.367 (<.0001*)	.293 (.005*)	.382 (<.0001*)	.317 (.002*)	.056 (.586)
Time Trail Making Test A	-.241 (-.016*)	-.569 (<.0001*)	1.000	.255 (.010*)	.703 (<.0001*)	.339 (<.0001*)	.101 (.318)	.257 (.009*)	.535 (<.0001*)	.223 (.026*)	.239 (.017*)	.366 (<.0001*)	.055 (.590)	.002 (.983)	.253 (.011*)	.399 (<.0001*)	-.111 (.274)	.387 (<.0001*)	-.190 (.069)	-.347 (<.0001*)	-.407 (<.0001*)	-.078 (.445)
Errors Trail Making Test A	-.077 (.449)	-.115 (.256)	.255 (.010*)	1.000	.248 (.023*)	.217 (.030*)	-.038 (.708)	.040 (.692)	.157 (.118)	.284 (.004*)	.016 (.874)	.301 (.002*)	.111 (.272)	.110 (.274)	.261 (.009*)	.087 (.388)	-.019 (.848)	.309 (.002*)	-.129 (.207)	-.094 (.367)	-.075 (.470)	-.018 (.858)
Time Trail Making Test B	-.217 (.030*)	-.554 (.<.0001*)	.703 (<.0001*)	.248 (.023*)	1.000	.621 (<.0001*)	.235 (.019*)	.186 (.064)	.523 (<.0001*)	.149 (.138)	.147 (.143)	.366 (<.0001*)	.143 (.155)	-.073 (.471)	.356 (<.0001*)	.314 (.001*)	-.206 (.040*)	.389 (<.0001*)	-.329 (.001*)	-.348 (<.0001*)	-.376 (<.0001*)	-.034 (.740)
Errors Trail Making Test B	.026 (.798)	-.298 (.003*)	.339 (<.0001*)	.217 (.030*)	.621 (<.0001*)	1.000	.106 (.292)	.082 (.416)	.397 (<.0001*)	.064 (.528)	.172 (.087)	.284 (.004*)	.162 (.108)	-.169 (.094)	.291 (.003*)	.158 (.117)	-.209 (.036*)	.237 (.018*)	-.174 (.087)	-.188 (.068)	-.174 (.091)	.073 (.479)
Uncorrec-ted Errors Trial 1 Stroop	.121 (.232)	-.104 (.304)	.101 (.318)	-.038 (.708)	.235 (.019*)	.106 (.292)	1.000	.173 (.086)	.184 (.067)	.095 (.349)	.039 (.707)	.036 (.728)	.204 (.042*)	-.101 (.315)	.007 (.947)	.239 (.017*)	.019 (.846)	.062 (.539)	.019 (.855)	-.079 (.448)	-.144 (.165)	.004 (.967)
Self-corrected Errors Trial 1 Stroop	-.129 (.198)	-.286 (.004*)	.257 (.009*)	.040 (.692)	.186 (.064)	.082 (.416)	.173 (.086)	1.000	.409 (<.0001*)	.108 (.287)	.259 (.009*)	.089 (.379)	.025 (.808)	.177 (.078)	.140 (.165)	.257 (.009*)	.210 (.036*)	.315 (.001*)	-.031 (.762)	-.153 (.139)	-.128 (.216)	-.006 (.952)
Time Trial 1 Stroop	-.118 (..241)	-.573 (<.0001*)	.535 (<.0001*)	.157 (.118)	.523 (<.0001*)	.397 (<.0001*)	.184 (.067)	.409 (<.0001*)	1.000	.043 (.671)	.344 (<.0001*)	.533 (<.0001*)	.139 (.166)	.174 (.083)	.545 (<.0001*)	.255 (.010*)	.024 (.814)	.548 (<.0001*)	-.084 (.412)	-.273 (.007*)	-.306 (.015*)	-.150 (.142)
Uncorrec-ted Errors Trial 2 Stroop	-.244 (.014*)	-.128 (.204)	.223 (.026*)	.284 (.004*)	.149 (.138)	.064 (.528)	.095 (.349)	.108 (.287)	.043 (.671)	1.000	.040 (.690)	.189 (.059)	.189 (.059)	.122 (.228)	.146 (.147)	.089 (.378)	-.092 (.361)	.066 (.517)	-.305 (.002*)	.012 (.906)	-.069 (.546)	-.024 (.815)

Table 7

Results of the Spearman's Rank-Order Correlations of the Various Neuropsychological Tests…Continuation Part A

Test Comp-onent	A1 RAVLT	B1 RAVLT	Time Trail Making Test A	Errors Trail Making Test A	Time Trail Making Test B	Errors Trail Making Test B	Uncorrec-ted Errors Trial 1 Stroop	Self-corrected Errors Trial 1 Stroop	Time Trial 1 Stroop	Uncorrec-ted Errors Trial 2 Stroop	Self-corrected Errors Trial 2 Stroop	Time Trial 2 Stroop	Uncorrec-ted Errors Trial 3 Stroop	Self-corrected Errors Trial 3 Stroop	Time Trial 3 Stroop	Uncorrec-ted Errors Trial 4 Stroop	Self-corrected Errors Trial 4 Stroop	Time Trial 4 Stroop	WISC-R Picture Complet-ion	WISC-R Digits Forward	WISC-R Digits Backward	WCST Failures To Maintain Set
Self-corrected Errors Trial 2 Stroop	.108 (.287)	-.236 (.018*)	.239 (.017*)	.016 (.874)	.147 (.143)	.172 (.087)	.039 (.707)	.259 (.009*)	.344 (<.0001*)	.040 (.690)	1.000	.474 (<.0001*)	.085 (.403)	.105 (.299)	.129 (.199)	.287 (.004*)	-.401 (.069)	.176 (.079)	.029 (.775)	-.173 (.094)	-.437 (<.0001*)	-.059 (.561)
Time Trial 2 Stroop	-.049 (.629)	-.338 (<.0001*)	.366 (<.0001*)	.301 (.002*)	.366 (<.0001*)	.284 (.004*)	.036 (.728)	.089 (.379)	.533 (<.0001*)	.189 (.059)	.474 (<.0001*)	1.000	.156 (.122)	.189 (.059)	.489 (<.0001*)	.048 (.639)	.099 (.329)	.487 (<.0001*)	-.100 (.328)	-.299 (.003*)	-.416 (<.0001*)	-.126 (.219)
Uncorrec-ted Errors Trial 3 Stroop	-.020 (.839)	.082 (.416)	.055 (.590)	.111 (.272)	.143 (.155)	.162 (.108)	.204 (.042*)	.025 (.808)	.139 (.166)	.189 (.059)	.085 (.403)	.156 (.122)	1.000	-.011 (.910)	.269 (.006*)	.265 (.008*)	-.153 (.129)	.091 (.368)	-.003 (.974)	-.082 (.421)	-.081 (.431)	.076 (.465)
Self-corrected Errors Trial 3 Stroop	-.069 (.497)	-.059 (.561)	.002 (.983)	.110 (.274)	-.073 (.471)	-.169 (.094)	-.101 (.315)	.177 (.078)	.174 (.083)	.122 (.228)	.105 (.299)	.189 (.059)	-.011 (.910)	1.000	.369 (<.0001*)	.017 (.870)	.317 (.001*)	.008 (.939)	-.408 (.639)	-.033 (.747)	-.076 (.455)	-.040 (.697)
Time Trial 3 Stroop	-.066 (.513)	-.333 (<.0001*)	.253 (.011*)	.261 (.009*)	.356 (<.0001*)	.291 (.003*)	.007 (.947)	.140 (.165)	.545 (<.0001*)	.146 (.147)	.129 (.199)	.489 (<.0001*)	.269 (.006*)	.369 (<.0001*)	1.000	.138 (.169)	.079 (.433)	.518 (<.0001*)	.050 (.623)	-.189 (.067)	-.224 (.027*)	-.061 (.556)
Uncorrec-ted Errors Trial 4 Stroop	-.065 (.521)	-.253 (.011*)	.399 (<.0001*)	.087 (.388)	.314 (.001*)	.158 (.117)	.239 (.017*)	.257 (.009*)	.255 (.010*)	.089 (.378)	.287 (.004*)	.048 (.639)	.265 (.008*)	.017 (.870)	.138 (.169)	1.000	-.141 (.161)	.282 (.004*)	-.141 (.169)	-.209 (.039*)	-.233 (.020*)	-.020 (.844)
Self-corrected Errors Trial 4 Stroop	.041 (.687)	.050 (.621)	-.111 (.274)	-.019 (.848)	-.206 (.040*)	-.209 (.036*)	.019 (.846)	.210 (.036*)	.024 (.814)	-.092 (.361)	-.401 (.069)	.099 (.329	-.153 (.129)	.317 (.001*)	.079 (.433)	-.141 (.161)	1.000	.306 (.002*)	.167 (.103)	-.069 (.498)	.042 (.678)	-.117 (.260)
Time Trial 4 Stroop	-.067 (.509)	-.367 (<.0001*)	.387 (<.0001*)	.309 (.002*)	.389 (<.0001*)	.237 (.018*)	.062 (.539)	.315 (.001*)	.548 (<.0001*)	.066 (.517)	.176 (.079)	.487 (<.0001*)	.091 (.368)	.008 (.939)	.518 (<.0001*)	.282 (.004*)	.306 (.002*)	1.000	-.036 (.729)	-.341 (<.0001*)	-.253 (.001*)	-.033 (.752)
WISC-R Picture Complet-ion	.186 (.068)	.293 (.005*)	-.190 (.069)	-.129 (.207)	-.329 (.001*)	-.174 (.087)	.019 (.855)	-.031 (.762)	-.084 (.412)	-.305 (.002*)	.029 (.775)	-.100 (.328)	-.003 (.974)	-.408 (.639)	.050 (.623)	-.141 (.169)	.167 (.103)	-.036 (.729)	1.000	.064 (.539)	.006 (.951)	.104 (.209)

Table 7

Results of the Spearman's Rank-Order Correlations of the Various Neuropsychological Tests…Continuation Part B

Test Comp-onent	A1 RAVLT	B1 RAVLT	Time Trail Making Test A	Errors Trail Making Test A	Time Trail Making Test B	Errors Trail Making Test B	Uncorrec-ted Errors Trial 1 Stroop	Self-corrected Errors Trial 1 Stroop	Time Trial 1 Stroop	Uncorrec-ted Errors Trial 2 Stroop	Self-corrected Errors Trial 2 Stroop	Time Trial 2 Stroop	Uncorrec-ted Errors Trial 3 Stroop	Self-corrected Errors Trial 3 Stroop	Time Trial 3 Stroop	Uncorrec-ted Errors Trial 4 Stroop	Self-corrected Errors Trial 4 Stroop	Time Trial 4 Stroop	WISC-R Picture Complet-ion	WISC-R Digits Forward	WISC-R Digits Backward	WCST Failures To Maintain Set
WISC-R Digits Forward	.246 (.015*)	.382 (<.0001*)	-.347 (<.0001*)	-.094 (.367)	-.348 (<.0001*)	-.188 (.068)	-.079 (.448)	-.153 (.139)	-.273 (.007*)	.012 (.906)	-.173 (.094)	-.299 (.003*)	-.082 (.421)	-.033 (.747)	-.189 (.067)	-.209 (.039*)	-.069 (.498)	-.341 (<.0001*)	.064 (.539)	1.000	.359 (<.0001*)	.025 (.809)
WISC-R Digits Backward	.162 (.111)	.317 (.002*)	-.407 (<.0001*)	-.075 (.470)	-.376 (<.0001*)	-.174 (.091)	-.144 (.165)	-.128 (.216)	-.306 (.015*)	-.069 (.546)	-.437 (<.0001*)	-.416 (<.0001*)	-.081 (.431)	-.076 (.455)	-.224 (.027*)	-.233 (.020*)	.042 (.678)	-.253 (.001*)	.006 (.951)	.359 (<.0001*)	1.000	.218 (.003)
WCST Failures To Maintain Set	.033 (.745)	.056 (.586)	-.078 (.445)	-.018 (.858)	-.034 (.740)	.073 (.479)	.004 (.967)	-.006 (.952)	-.150 (.142)	-.024 (.815)	-.059 (.561)	-.126 (.219)	.076 (.465)	-.040 (.697)	-.061 (.556)	-.020 (.844)	-.117 (.260)	-.033 (.752)	.104 (.209)	.025 (.809)	.218 (.003)	1.000

Note. *p < .05

As can be seen from the table above, the WISC-R Digit Span Forward subtest was found to correlate significantly and positively, and the strength of the correlation was weak, with both trials A1 and B1 of the RAVLT. That is, as performance on the WISC-R Digit Span Forward subtest increased, so did performance on trials A1 and B1 of the RAVLT. This result indicates that each of these measurements assess the same or a similar construct.

The WISC-R Digit Span Forward subtest was found to correlate significantly and negatively, and the strength of the correlation was weak, with the time taken on trial 1; the time taken on trial 2; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on the WISC-R Digit Span Forward subtest increased, the time taken on these trials of the Stroop Colour-Word Interference Test decreased. An increased number of digits correctly repeated in sequence on the former measure, the WISC-R Digit Span Forward subtest, indicates a better performance by the participants. In contrast, a reduced time on the latter measure, the Stroop Colour-Word Interference Test, indicates a better performance by the participants. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Digit Span Forward subtest was found to correlate significantly and negatively, and the strength of the correlation was weak, with the uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test; and the self-corrected errors on trial 2 of the Stroop Colour-Word Interference Test. In other words, as performance on the WISC-R Digit Span Forward subtest increased, the number of errors on the trials of the Stroop Colour-Word Interference Test decreased. A fewer number of errors on the Stroop Colour-Word Interference Test is in keeping with better performance. Thus, these results indicate that each of these measurements assess the same or a similar construct.

Trial A1 of the RAVLT was found to correlate significantly and positively, and the strength of the correlation was weak, with trial B1 of the RAVLT. This means that as the participants obtained better scores on trial A1, they also obtained better scores on trial B1 of the RAVLT, which is to be expected. This result indicates that each of these measurements assess the same or a similar construct.

Trial A1 of the RAVLT was found to correlate significantly and negatively, and the strength of the correlation was weak, with the number of uncorrected errors on trial 2 of the Stroop Colour-Word Interference Test. In other words, as performance on trial A1 of the RAVLT increased, the number of uncorrected errors on trial 2 of the Stroop Colour-Word Interference Test decreased. A fewer number of errors on the Stroop Colour-Word Interference Test is in keeping with better performance. Thus, these results indicate that each of these measurements assess the same or a similar construct.

Trial B1 of the RAVLT was found to correlate significantly and positively, and the strength of the correlation was weak, with the WISC-R Picture Completion subtest. That is, as performance on Trial B1 of the RAVLT increased, performance on the WISC-R Picture Completion subtest also increased. Thus, this result indicates that each of these measurements assess the same or a similar construct.

Trial B1 of the RAVLT was found to correlate significantly and negatively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the number of self-corrected errors on trial 2; and the number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on Trial B1 of the RAVLT increased, performance on the Stroop Colour-Word Interference Test decreased. As noted, fewer errors on the Stroop Colour-Word Interference Test is in keeping with better performance. Thus, this result indicates that each of these measurements assess the same or a similar construct.

Trial B1 of the RAVLT was found to correlate significantly and negatively, and the strength of the correlation was medium, with the time taken on trial 1 of the Stroop Colour-Word Interference Test. That is, as performance on Trial B1 of the RAVLT increased, performance on the Stroop Colour-Word Interference Test decreased. A higher number of words recalled on trial B1 of the RAVLT is in keeping with better performance, whilst a shorter time to complete the Stroop Colour-Word Interference Test is in keeping with better performance. Thus, this result indicates that each of these measurements assess the same or a similar construct.

Trial B1 of the RAVLT was found to correlate significantly and negatively, and the strength of the correlation was weak, with the time taken on trial 2; the time taken on trial 3; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on Trial B1 of the RAVLT increased, performance on the Stroop Colour-Word Interference Test decreased. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on the Trail Making Test Part A was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors made on trial 2 of the Stroop Colour-Word Interference Test. In other words, as participants slowed when completing the Trail Making Test Part A, they made a higher number of errors. This may imply that the participants were making more errors as a consequence of having difficulty dividing their attention to complete the test, and indicates that each of these measurements assess the same or a similar construct.

The number of errors made on the Trail Making Test Part A was found to correlate significantly and positively, and the strength of the correlation was weak, with the time taken on trial 1 of the Stroop

Colour-Word Interference Test. In other words, as participants made more errors on the Trail Making Test Part A, they took longer to complete trial 1 of the Stroop Colour-Word Interference Test. This indicates that each of these measurements assess the same or a similar construct.

The time taken on the Trail Making Test Part B was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of errors made on Trail Making Test Part B and the number of uncorrected errors on trial 1 of the Stroop Colour-Word Interference Test. In other words, as participants slowed when completing the Trail Making Test Part B, they made a higher number of errors on the relevant tests. This indicates that each of these measurements assess the same or a similar construct.

The number of errors made on the Trail Making Test Part B was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1, 2 and 4; and the number of uncorrected errors on trial 2 and 4 of the Stroop Colour-Word Interference Test. In other words, as participants made more errors on the Trail Making Test Part B, they made more errors on the relevant trials of the Stroop Colour-Word Interference Test. This indicates that each of these measurements assess the same or a similar construct.

The number of self-corrected errors on trial 1 of the Stroop Colour-Word Interference Test was found to correlate significantly and positively, and the strength of the correlation was weak, with the time taken on trial 1; the number of self-corrected errors on trial 2; the number of self-corrected errors on trial 3; the time taken on trial 3; the number of uncorrected errors on trial 4; the number of self-corrected errors on trial 4; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 1 of the Stroop Colour-Word Interference Test was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of uncorrected errors on trial 3 and 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, this result indicates that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 1 of the Stroop Colour-Word Interference Test was found to correlate significantly and negatively, and the strength of the correlation was weak, with the WISC-R Digits backward subtest. That is, as participants made more errors on this aspect of the Stroop Colour-

Word Interference Test increased, they were able to repeat shorter strings of digits, in keeping with poor performance on both measures. Thus, this result indicates that each of these measurements assess the same or a similar construct.

The time taken on trial 1 of the Stroop Colour-Word Interference Test was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the number of self-corrected errors on trial 2; the number of uncorrected errors on trial 4; the time taken on trial 2; and the time taken on trial 3 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 1 was found to significantly correlate with the time taken on trial 4 of the Stroop Colour-Word Interference Test. The correlation was in a positive direction and the strength of the correlation was medium. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspect of the test. Thus, this result indicates that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 2 was found to correlate significantly and negatively, and the strength of the correlation was weak, with the WISC-R Picture Completion subtest. That is, as participants made more errors on this aspect of the Stroop Colour-Word Interference Test, participants achieved lower raw scores on the WISC-R Picture Completion subtest, in keeping with poorer performance on both measures. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of self-corrected errors on trial 2 was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the time taken on trial 1; and the number of uncorrected errors on trial 4. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of self-corrected errors on trial 2 was found to significantly correlate with the time taken on trial 2 of the Stroop Colour-Word Interference Test. The correlation was in a positive direction and the strength of the correlation was medium. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspect of the test. Thus, this result indicates that each of these measurements assess the same or a similar construct.

The time taken on trial 2 was found to correlate significantly and positively, and the strength of the correlation was medium, with the time taken on trial 1; and the number of self-corrected errors on trial 2 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 2 was found to correlate significantly and positively, and the strength of the correlation was weak, with the time taken on trial 3; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results would indicate that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 3 was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of uncorrected errors on trial 1; the time taken on trial 3; and the number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of self-corrected errors on trial 3 was found to correlate significantly and positively, and the strength of the correlation was weak, with the time taken on trial 1; the time taken on trial 3; and the number of self-corrected errors on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 3 was found to correlate significantly and positively, and the strength of the correlation was weak, with the time taken on trial 2; the number of uncorrected errors on trial 3; and the number of self-corrected errors on trial 3 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 3 was found to correlate significantly and positively, and the strength of the correlation was medium, with the time taken on trial 1; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word

Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 4 was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the number of self-corrected errors on trial 2; the number of uncorrected errors on trial 3; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test was found to correlate significantly and negatively, and the strength of the correlation was weak, with the WISC-R Digits Backward subtest. That is, as participants made more errors on this aspect of the Stroop Colour-Word Interference Test increased, participants were able to repeat shorter strings of digits on the WISC-R Digits Backward, in keeping with poorer performance. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The number of self-corrected errors on trial 4 was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the number of self-corrected errors on trial 3; and the time taken on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 4 was found to correlate significantly and positively, and the strength of the correlation was weak, with the number of self-corrected errors on trial 1; the time taken on trial 2; and the number of self-corrected errors on trial 4 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The time taken on trial 4 was found to correlate significantly and positively, and the strength of the correlation was medium, with the time taken on trial 1; and the time taken on trial 3 of the Stroop Colour-Word Interference Test. That is, as performance on one aspect of the Stroop Colour-Word Interference Test increased, so did performance on the other aspects of the test. Thus, these results indicate that each of these measurements assess the same or a similar construct.

The correlations between the remaining tests were non-significant.

9.2.5 Pearson's Product Moment Correlations between the Two Samples on the Neuropsychological Tests

In order to investigate one of the specific aims of the current research study, that is, to identify group differences of attention and concentration functions between adolescents with HIV, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, and a contrast group of HIV-negative adolescents, Pearson's Product Moment Correlations were run on the normally distributed data, comparing the results of the HIV-positive and HIV-negative participants on each of the dependent variables, as operationalised as scores on the various neuropsychological tests. The results of these Pearson's Product Moment Correlations are outlined in Table 8 below.

Table 8

Results of the Pearson's Product Moment Correlations of the Various Neuropsychological Tests

Test Component	WISC-R Coding subtest
RAVLT Trial A1	.213 (.036*)
RAVLT Trial B1	.230 (.022*)
Time taken on Trail Making Test Part A	-.416 (<.0001*)
Number of errors on Trail Making Test Part A	-.130 (.202)
Time taken on Trail Making Test Part B	-.442 (<.0001*)
Number of errors on Trail Making Test Part B	-.321 (.001*)
Uncorrected errors on trial 1 of the Stroop Colour-Word Interference Test	-.136 (.18)
Self-corrected errors on trial 1 of the Stroop Colour-Word Interference Test	-.110 (.280)
Time taken on trial 1 of the Stroop Colour-Word Interference Test	-.277 (.006*)
Uncorrected errors on trial 2 of the Stroop Colour-Word Interference Test	-.272 (.007*)
Self-corrected errors on trial 2 of the Stroop Colour-Word Interference Test	-.140 (.168)
Time taken on trial 2 of the Stroop Colour-Word Interference Test	-.239 (.018*)
Uncorrected errors on trial 3 of the Stroop Colour-Word Interference Test	-.072 (.483)
Self-corrected errors on trial 3 of the Stroop Colour-Word Interference Test	-.05 (.659)
Time taken on trial 3 of the Stroop Colour-Word Interference Test	-.095 (.349)
Uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test	-.286 (.004*)
Self-corrected errors on trial 4 of the Stroop Colour-Word Interference Test	.090 (.376)
Time taken on trial 4 of the Stroop Colour-Word Interference Test	-.244 (.015*)
WISC-R Picture Completion subtest	.205 (.050)
WISC-R Digit Span Forward subtest	.228 (.024*)
WISC-R Digit Span Backward subtest	.295 (.003*)
WCST Number of failures to maintain set	-.040 (.698)

Note. *p < .05

The WISC-R Coding subtest was found to correlate significantly with the RAVLT Trial A1. The correlation was in a positive direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants made were able to recall more words on this trial of the RAVLT. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the RAVLT Trial B1. The correlation was in a positive direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants made were able to recall more words on this trial of the RAVLT. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the time taken on the Trail Making Test Part A. The correlation was in a negative direction and the strength of the correlation was moderate. Thus, as performance increased on the WISC-R Coding subtest, participants completed this trial of the task faster. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the time taken on the Trail Making Test Part B. The correlation was in a negative direction and the strength of the correlation was moderate. Thus, as performance increased on the WISC-R Coding subtest, participants completed this trial of the task faster. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the number of errors made on the Trail Making Test Part B. The correlation was in a negative direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants made fewer errors on this trial of the test. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the time taken on trial 1 of the Stroop Colour-Word Interference Test. The correlation was in a negative direction and the strength of

the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants completed this trial of the Stroop Colour-Word Interference Test quicker. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the time taken on trial 2 of the Stroop Colour-Word Interference Test. The correlation was in a negative direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants completed this trial of the Stroop Colour-Word Interference Test quicker. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the time taken on trial 4 of the Stroop Colour-Word Interference Test. The correlation was in a negative direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants completed this trial of the Stroop Colour-Word Interference Test quicker. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the number of uncorrected errors on trial 2 of the Stroop Colour-Word Interference Test. The correlation was in a negative direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants made fewer errors on the Stroop Colour-Word Interference Test. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test. The correlation was in a negative direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants made fewer errors on the Stroop Colour-Word Interference Test. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the WISC-R Digit Span Forward subtest. The correlation was in a positive direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants were able to recall longer strings of Digits on this trial of the test. Both of these results are in keeping with better

performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The WISC-R Coding subtest was found to correlate significantly with the WISC-R Digit Span Backward subtest. The correlation was in a positive direction and the strength of the correlation was weak. Thus, as performance increased on the WISC-R Coding subtest, participants were able to recall longer strings of Digits on this trial of the test. Both of these results are in keeping with better performance on the respective measures. Therefore, these results indicate that each of these measurements assess the same or a similar construct.

The correlations between the remaining tests were non-significant.

9.2.6 The Impact of the Various Clinical Variables of the HIV-Positive Participants on the Neuropsychological Test Results

In order to investigate the impact of the various clinical variables of the HIV-positive participants, such as the age at which HAART was commenced; the duration of ARV treatment; the WHO stage at diagnosis; the starting and current $CD4^+$ counts; and the starting and current viral loads, Student's t-Tests and Mann-Whitney U Tests were run on the neuropsychological test results. The results of these Student's t-Tests and Mann-Whitney U Tests are outlined in Table 9 below.

Table 9

Results of the Student's t-Tests and Mann-Whitney U Tests Showing the Impact of the Various Clinical Variables of the HIV-Positive Participants on the Neuropsychological Test Results

Test	Dependent Variable	Age HAART was started	Years on HAART	WHO stage at diagnosis	Starting $CD4^+$ count	Current $CD4^+$ count	Starting viral load	Current viral load
RAVLT	Number of words recalled on trial A1	U = 236 (.002*)	U = 435 (.830)	U = 102 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Number of words recalled on trial B1	U = 193 (<.0001*)	U = 376 (.277)	U = 156.5 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	*U* = 0 (<.0001*)	U = 0 (<.0001*)
WCST	Number of failures to maintain set	U = 18 (<.0001*)	U = 22.59.43 (<.0001*)	U = 74 (<.0001*)	U = 0 (<.000*)	U = 0 (<.0001*)	U = 0 (<.0001*)	*U* = 0 (<.0001*)
Stroop Colour-Word Interference Test	Time taken on trial 1	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 90 (<.0001*)	U = 60.5 (<.0001*)	U = 101.5 (<.0001*)	U = 282.5 (.384)
	Number of uncorrected errors on trial 1	U = 31 (<.0001*)	U = 50 (<.0001*)	U = 140 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Number of self-corrected errors on trial 1	U = 50 (<.0001*)	U = 100.5 (<.0001*)	*U* = 260 (.021*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)

Table 9

Results of the Student's t-Tests and Mann-Whitney U Tests Showing the Impact of the Various Clinical Variables of the HIV-Positive Participants on the Neuropsychological Test Results…Continuation Part A

Test	Dependent Variable	Age HAART was started	Years on HAART	WHO stage at diagnosis	Starting $CD4^+$ count	Current $CD4^+$ count	Starting viral load	Current viral load
Stroop Colour-Word Interference Test	Time taken on trial 2	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	*U* = 84 (<.0001*)	U = 43 (<.0001*)	U = 87 (<.0001*)	U = 133.5 (.0002*)
	Number of uncorrected errors on trial 2	U = 12 (<.0001*)	U = 14 (<.0001*)	U = 44 (<.0001*)	U = 0 (<.0001*)	*U* = 0 (<.0001*)	U = 0 (<.0001*)	*U* = 0 (<.0001*)
	Number of self-corrected errors on trial 2	U = 34 (<.0001*)	U = 58.5 (<.0001*)	U = 165.5 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Time taken on trial 3	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 137.5 (<.0001*)	U = 87 (<.0001*)	U = 119 (<.0001*)	U = 284.51.72 (.405)
	Number of uncorrected errors on trial 3	U = 180.5 (<.0001*)	U = 262 (.006*)	U = 390.5 (.823)	U = 2 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	*t* = 0 (<.0001*)
	Number of self-corrected errors on trial 3	U = 171.5 (<.0001*)	U = 283 (.014*)	U = 333 (.253)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Time taken on trial 4	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 140 (<.0001*)	U = 89 (<.0001*)	U = 119 (<.0001*)	U = 284.52 (.405)

Table 9

Results of the Student's t-Tests and Mann-Whitney U Tests Showing the Impact of the Various Clinical Variables of the HIV-Positive Participants on the Neuropsychological Test Results…Continuation Part B

Test	Dependent Variable	Age HAART was started	Years on HAART	WHO stage at diagnosis	Starting $CD4^+$ count	Current $CD4^+$ count	Starting viral load	Current viral load
Stroop Colour-Word Interference Test	Number of uncorrected errors on trial 4	U = 265 (.006*)	U = 382.5 (.322)	U = 257.5 (.019*)	U = 1 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Number of self-corrected errors on trial 4	U = 117.5 (<.0001*)	U = 205 (.0003*)	*U* = 385.5 (.761)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
Trail Making Test	Time taken on Part A	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 103 (<.0001*)	U = 68.5 (<.0001*)	U = 110.5 (<.0001*)	U = 317 (.817)
	Time taken on Part B	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 212.5 (.0004*)	U = 89 (<.0001*)	U = 124 (<.0001*)	U = 260.5 (.201)
WISC-R Coding Subtest	Raw Score	*t* = 16.089 (<.0001*)	*t* = 16.984 (<.0001*)	*t* = 18.187 (<.0001*)	*t* = -2.552 (.013*)	*t* = -11.738 (<.0001*)	*t* = -3.197 (<.0001*)	*t* = -1.689 (.097)
WISC-R Picture Completion Subtest	Raw Score	U = 54.5 (<.0001*)	U = 23 (<.0001*)	U = 0 (<.0001*)	U = 31 (<.0001*)	U = 1 (<.0001*)	U = 0 (<.0001*)	*U* = 0 (<.0001*)

Table 9

Results of the Student's t-Tests and Mann-Whitney U Tests Showing the Impact of the Various Clinical Variables of the HIV-Positive Participants on the Neuropsychological Test Results…Continuation Part C

Test	Dependent Variable	Age HAART was started	Years on HAART	WHO stage at diagnosis	Starting $CD4^+$ count	Current $CD4^+$ count	Starting viral load	Current viral load
WISC-R Digit Span Subtest	Items reproduced on Digits Forward	U = 143.5 (<.0001*)	U = 314.5 (.069)	U = 159.5 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)
	Items reproduced on Digits Backward	U = 69 (<.0001*)	U = 162 (<.0001*)	U = 379.5 (.850)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)	U = 0 (<.0001*)

Note. *p < .05

As can be seen from the table above, the age at which HAART was commenced significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2, 3 and 4; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; the WISC-R Digit Span Forward subtest and the WISC-R Digit Span Backward subtest.

The duration of ARV treatment significantly impacted on the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2 and 3; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; and the WISC-R Digit Span Backward subtest.

The WHO stage at diagnosis significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2 and 4; and the number of self-corrected errors on trials 1 and 2 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; and the Digit Span Forward subtest.

The starting $CD4^+$ count significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2, 3 and 4; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; the WISC-R Digit Span Forward subtest; and the WISC-R Digit Span Backward subtest.

The current $CD4^+$ count significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2, 3 and 4; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; the WISC-R Digit Span Forward subtest; and the WISC-R Digit Span Backward subtest.

The starting viral load significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1, 2, 3 and 4; the number of uncorrected errors on trials 1, 2, 3 and 4; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the time taken on the Trail Making Test Part A; the time taken on the Trail Making Test Part B; the WISC-R Picture Completion subtest; the WISC-R Coding subtest; the WISC-R Digit Span Forward subtest; and the WISC-R Digit Span Backward subtest.

The current viral load significantly impacted on trial A1 of the RAVLT; trial B1 of the RAVLT; the number of failures to maintain set on the WCST; the time taken on trials 1 and 2; the number of uncorrected errors on trials 1, 2, 3 and 4; and the number of self-corrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test; the WISC-R Picture Completion subtest; the WISC-R Digit Span Forward subtest; and the WISC-R Digit Span Backward subtest.

The remainder of the comparisons of the clinical variations in the HIV-positive sample were not significantly different from each other.

10. Discussion

Previous studies have asserted that Human Immunodeficiency Virus (HIV) infection is associated with difficulties in attention (Law et al., 1994; Martin et al., 1992; Sorenson et al., 1994). The current research set out to answer the question as to what the characteristics of attention and concentration are in a sample of HIV-positive adolescents, who were commenced on managed anti-retroviral (ARV) programmes following diagnosis of HIV and immune compromise, in comparison with an equivalent sample of HIV-negative adolescents. In order to do so, each category of attention, including verbal and visual focused attention, and verbal and visual divided attention, was understood as the data that resulted from the scores on specific neuropsychological tests. These tests included trials A1 and B1 of the Rey Auditory Verbal Learning Test (RAVLT), the number of failures to maintain set on the Wisconsin Card Sorting Test (WCST), the time taken and the number of errors made on the Stroop Colour-Word Interference Test, the time taken and the number of errors made on the Trail Making Test, the Wechsler Intelligence Scale for Children – Revised (WISC-R) Coding subtest, the WISC-R Digit Span subtest, and the WISC-R Picture Completion subtest. The performance of the HIV-positive and HIV-negative participants in each category of attention, including verbal and visual focused attention, and verbal and visual divided attention, was then compared by means of Pearson's Product-Moment Correlation Coefficients and Spearman's Rank-Order Correlation Coefficients. The results are discussed below.

The Stroop Colour-Word Interference Test appeared to provide the majority of the significant results on the comparisons that were run between the two samples on the neuropsychological tests. Importantly, the number of uncorrected errors, and the number of self-corrected errors on trial 3 were all significantly different between the two samples, with the HIV-positive participants performing worse than the HIV-negative participants. On trial 3 of the Stroop Colour-Word Interference Test, participants are required to inhibit an automatic response and instead, give a different response. The participants have to keep this rule active in mind in order to complete the task as quickly and correctly as possible. Furthermore the HIV-positive participants made a significantly higher number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test than did the HIV-negative participants. Similarly to trial 3 of the Stroop Colour-Word Interference Test, on trial 4 participants are required to divide their attention and provide one of two appropriate responses: either to inhibit an automatic response and instead, give a different response, or to merely provide the automatic response. The participants have to keep this rule active in mind in order to complete the task as quickly and correctly as possible. Other findings of the current study were that the HIV-positive participants made a significantly higher number of uncorrected errors on trials 1 and 2; and self-corrected errors on trials 1 and 2 of the Stroop Colour-Word Interference Test than did the HIV-

negative participants. Also, the HIV-positive participants completed trial 1 of the Stroop Colour-Word Interference Test significantly slower than did the HIV-negative participants. On trial 1 of the Stroop Colour-Word Interference Test, participants are required to name colours, whilst trial 2 demands that participants read words, both as quickly as possible.

The slower time taken to complete trial 1 of the Stroop Colour-Word Interference Test implies that the HIV-positive participants had more difficulty than the HIV-negative participants providing automatic responses to successfully complete this task as quickly as possible and they were slower to process the information. The ability to focus cognitive resources to read as quickly as possible on this test provides a measure of verbal focused attention.

A high number of self-corrected errors on trials 1, 2 and 3 of the Stroop Colour-Word Interference Test implies that the HIV-positive participants were trying to read the words and name the colours too quickly. Thus, they made errors of which they were aware, and subsequently corrected, on trial 1 and 2; whilst on trial 3, the HIV-positive participants were unable to inhibit automatic responses to successfully complete this task with as few mistakes as possible, but they noted and subsequently self-corrected their errors. As can be seen, the rules of the trials were held active in mind by the participants. The ability to shift cognitive response set and to inhibit an over-learned response provides a measure of verbal focused attention.

A high number of uncorrected errors on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test implies that the HIV-positive participants were trying to read the words and name colours as quickly as possible, but that they were engaged with the task on a superficial level and thus, did not notice their errors on trials 1 and 2; whilst on trial 3 and 4, the participants were unable to monitor their own errors. The ability to monitor one's own performance provides another measure of verbal focused attention.

The results of this study imply that these functions are significantly more difficult for HIV-positive individuals; the time, number of self-corrected errors and number of uncorrected errors were all consistently poorer in the HIV-positive participants than in the HIV-negative participants. Furthermore, in order to achieve the goal of the trials, which is to perform them as fast as possible, healthy individuals may sacrifice accuracy, leading to a higher number of errors. This was not the case with the HIV-positive participants who made both a high number of errors and completed the task more slowly than did the HIV-negative participants.

The results of the current study may indicate that trial 1 of the Stroop Colour-Word Interference Test, including the time taken, as well as the number of uncorrected errors and the number of self-corrected

errors made, appears to be a good measure to assess verbal focused attention. Additionally, despite the fact that methodological limitations of the current study, including small sample sizes, were present, trial 1 of the Stroop Colour-Word Interference Test still appeared to be a sensitive measure of attention difficulties. However, the testing environments of the HIV-positive and HIV-negative groups were heterogeneous with the HIV-negative participants being tested individually but in a group environment, whilst the HIV-positive participants were tested in individual, private offices. Because this factor affected performance on this measure differentially to the other measures utilised in this study, it is possible that the current results are indicative of another factor, such as slowed speed of processing, and not that of attention. If the HIV-negative participants had been tested in individual, private offices, they may have performed differently (or better) than they did in the current study, and hypothetically, the results may not indicate attention deficits; especially as the testing environment for the HIV-negative participants was less facilitating of good attention. This may imply that trial 1 of the Stroop Colour-Word Interference Test was not detecting a consistent attention issue that was specifically related to HIV status. Given the design of the test, this trial may have been detecting speed of processing instead, and it may be that this function is more sensitive to HIV status than attention as operationalised by trial 1. Furthermore, given the design of the test, trials 2, 3 and 4 may have detected general slowing effects, and it may be that this function is more sensitive to HIV status than is attention (Davidson et al., 2007).

This hypothesis is supported by a meta-analysis of 19 studies. Specifically, investigation of the Stroop Colour-Word Interference Test scores revealed worse performance for Attention Deficit Hyperactivity Disorder (ADHD) groups relative to the control groups. The authors concluded that performance, as measured by the time taken on trial 1, is consistently compromised in individuals with ADHD, likely due to attention deficits (Lansbergen et al., 2007).

In a similar study, performance on the Stroop Colour-Word Interference Test of 36 boys with a diagnosis of ADHD, which was compared with performances of a matched control sample, was poorer than the control group on both the control (trials 1 and 2) and the interference (trials 3 and 4) conditions of the Stroop Colour-Word Interference Test (Savitz & Jansen, 2003). The fundamental feature of the ADHD group was attention deficits, which was thought to underlie the slower performance on these trials of the Stroop Colour-Word Interference Test.

Based on the results of the current study compared to these two previous investigations, it is possible that the HIV-positive participants behaved similarly on the Stroop Colour-Word Interference Test as did the ADHD participants in the previous studies. The findings are comparable, as all of the studies examined the effects of attention difficulties on test performance; thus, it is possible to explain the

results of the current study on the basis of an attention deficit in the HIV-positive sample, even if the attention deficit is not necessarily a disorder as is ADHD in the previous studies.

Tying the above-mentioned information together, the HIV-positive participants performed worse on trials 1, 2, 3 and 4 of the Stroop Colour-Word Interference Test, and whilst it appears, on the basis of previous investigations, that individuals with ADHD also perform poorly on these trials of the test, it is possible that the HIV-positive participants were displaying an attention deficit that was measured by this task. However, this remains to be proved conclusively, as the current research study was subject to environmental factors that may explain the difference in performance between the HIV-positive and HIV-negative participants on the basis of another reason, such as general slowing, response inhibition and/or interference control.

Other relevant results shown by the current study relate to the Trail Making Test Parts A and B. Specifically, the results showed that the HIV-positive participants made a significantly higher number of errors on the Trail Making Test Parts A and B, and completed Part A slower, than did the HIV-negative participants. Part A requires participants to join numbers in order, which requires focused visual attention. Part B requires participants to alternate between letters and numbers in the correct order; this means that they are required to mentally manipulate information. Thus, this test is assumed to provide a measure of visual divided attention. The results on this measure indicated that the HIV-positive participants had difficulties with visual focused and divided attention; the HIV-positive participants had difficulty processing information, keeping track of the task they were doing, processing two streams of information simultaneously and making their performance as accurate as possible.

The findings of the current study are, in essence, similar to the results of a previous study by Cohen et al. (2011); however, the current study found significant results related to both time and errors, whilst the previous study found that speed on the test was the significant factor. Specifically, the authors hypothesised that performance on measures of attention, including the Trail Making Test Parts A and B, would be affected in HIV-infected individuals. The speeds of completion of the participants on these tasks were found to be affected in HIV-positive participants.

This particular result of the current study indicates that an adequate measure to assess attention appears to be the number of errors made on the Trail Making Test Parts A and B, and the time taken to complete Part A. However, the testing environments of the HIV-positive and HIV-negative groups were different. It is again possible that the current results are indicative of a factor other than attention. This may imply that the number of errors made on the Trail Making Test Part Parts A and B, and the time taken to complete Part A are not detecting attention difficulties that are specifically

related to HIV status. Instead, the number of errors made on the Trail Making Test Parts A and B may have been indicating difficulties with self-monitoring rather than difficulties with attention; and the slower speed on Part A may have been in keeping with slowed speed of processing. That is, the results of the present study superficially imply that the findings were due to an attention issue, but due to the testing conditions, this might not be the case. This result may be in keeping with the findings on the Stroop Colour-Word Interference Test; specifically, it is possible that the participants have difficulty inhibiting automatic responses and that they may be reverting to the familiar, over-learned sequence of letters or numbers. The participants may merely be putting numbers and/or letters in sequence, which is automatic, as opposed to alternating between the two, which is the test requirement. As a result of this, the participants committed errors. Additionally, slowed speed of processing may be associated with an increased number of errors. Specifically, in a previous study, it was noted that older adults show a greater increase in the number of errors than do younger adults. This was attributed to general slowing effects in older adults and to age deficits in particular cognitive processes, including inhibition and frontal lobe dysfunction (Davidson et al., 2007).

Other relevant results shown by the current study relate to the number of words recalled on trial B1 of the RAVLT. Specifically, the results showed that the HIV-positive participants recalled significantly fewer words than did the HIV-negative participants. This trial requires participants to attend to and repeat verbally-provided information, which requires focused verbal attention. The results on this measure indicated that the HIV-positive participants had difficulties with verbal focused attention; the HIV-positive participants had difficulty attending to the information, and repeating it back to the examiner, especially in the context of the interfering effects of having just learnt a different set of verbally-administered information.

The last relevant finding of the current study relate to the speed at which the WISC-R Coding subtest was completed. Specifically, the results showed that the HIV-positive participants completed this test significantly slower than did the HIV-negative participants. This trial requires participants to attend to visual information, and match symbols and numbers as quickly as possible, which requires focused visual attention. The results on this measure indicated that the HIV-positive participants had difficulties with visual focused attention.

As can be seen from the above-mentioned information, there were a few, circumscribed tests that provided significant results in terms of differential attentional functioning in HIV-positive and HIV-negative individuals, whilst many commonly-utilised tests of attention failed to reveal significant findings. Given this, it was imperative to revisit the operational definitions used in this study and to elucidate the manner in which the tests functioned in the two samples in terms of their core function and what they intended to measure. That is, it was necessary to investigate whether the

neuropsychological tests that purportedly and theoretically measure various aspects of attention were indeed correlated, implying that they were measuring the same construct. Specifically, the performance of the HIV-positive and the HIV-negative samples on the neuropsychological tests was examined in order to assess how consistent the various measures were between the groups in evaluating attention, and whether something other than this may be affecting the results, such as administration discrepancies and small sample size; this provided an indication of the construct validity of each of the measures. The current research attempted to assess a specific construct, attention, with more than one measurement/neuropsychological test, but performance on only some of the measures showed a difference between the groups. Based on this, it is possible that these measures were not assessing the same construct in the two samples. This is examined further below.

Trial A1 of the RAVLT correlated with only some of the other measures of attention, whilst trial B1 of the RAVLT correlated with many of the other measures of attention. Both Trials A1 and B1 of the RAVLT are assumed to assess verbal focused attention. However, trial B1, given the design of the test, has a proactive interference effect: participants are required to learn and pay attention to other information first; that is, participants have to learn (or attend) while prior learning is activated, which may play an interference role. Thus, trial B1 appeared to be a better measure of verbal focused attention than trial A1: prior learning/interference effects make trial B1 load more than does trial A1 in this regard.

In order to investigate the use of trials A1 and B1 of the RAVLT as a measure of attention, a study was conducted to investigate selective attention in patients with amyotrophic lateral sclerosis (ALS) and to examine the contribution of selective attention to patients' verbal free recall on these trials of the RAVLT (Christidi et al., 2012). The authors examined 22 non-demented patients with sporadic ALS and 22 demographically-related controls. Selective attention was found to influence immediate verbal free recall on trials A1 and B1 of the RAVLT. Thus, the previous study supports the findings of the current study, and trials A1 and B1 of the RAVLT appear to measure the same construct of verbal focused attention, with trial B1 being a more sensitive measure in this regard.

The time taken and the number of uncorrected and self-corrected errors on trials 1 to 4 of the Stroop Colour-Word Interference Test were included as indications of verbal focused attention. The time taken, and the number of uncorrected and self-corrected errors on trial 3 of the Stroop Colour-Word Interference Test provides an indication of active verbal focused attention; participants are required to inhibit an automatic response and, instead, make a different response by actively attending to the task. The WISC-R Digit Span Forward subtest was found to be related to the number of uncorrected errors on trial 3 of the Stroop Colour-Word Interference Test. The WISC-R Digit Span Forward subtest provides an indication of passive verbal focused attention based on the design of the test; the

participants are required to attend to numbers and reproduce them. The results of the current study indicated that the WISC-R Digit Span Forward subtest, and the time taken, and the number of errors on trial 3 of the Stroop Colour-Word Interference Test provided good indications of active verbal focused attention.

Trial 4 of the Stroop Colour-Word Interference Test is a difficult trial in which participants must actively mentally manipulate information. The elevated number of uncorrected errors on trial 4 by the participants confirms that this is a hard trial and implies that the participants were not processing information at a deep level. The results revealed that the time taken on trial 4 was found to relate with many other tests; these measures appear to be measuring the same construct of verbal focused attention. However, the time taken on trial 4 did not relate to trial A1 of the RAVLT or the number of uncorrected errors on trials 1 to 4 of the Stroop Colour-Word Interference Test: it would be interesting to study this effect in future research investigations. It is possible that this finding may be suggesting that trial 4 requires active processing, whilst trial A1 of the RAVLT require passive processing. Active processing refers to sets of procedures in which an individual acts on instructional inputs to generate, re-organise, self-explain, or otherwise goes beyond the encoding of presented material. Active processing in learning or testing may result in more learning. Conversely, passive processing does not involve the expenditure of additional energy or effort (Lezak, 1995). It stands to reason that if individuals are engaged in passive processing when active processing is required, then a higher number of errors are committed; and this may be the case in this regard.

Based on the design of the test, the WISC-R Digit Span Backward subtest is presumed to provide an indication of active verbal divided attention; the participants are required to attend to numbers and reverse them. The Trail Making Test Part B is presumed to provide an indication of active visual divided attention based on the design of the test; the participants are required to alternate between letters and numbers in the correct order. In the current study, the WISC-R Digit Span Backward subtest was shown to correlate with the time taken on the Trail Making Test Part B. This indicates that these measures are adequate indicators of divided attention.

The relationship between ADHD and the WISC-R Digit Span Backward subtest test performance was examined in a previous study. Hyperactivity/attentional problems were measured by the Hyperactivity scale of the Child Behavior Checklist. Performance on a neuropsychological task thought to contain an attentional component, the WISC-R Digit Span subtest, was used to operationalise attention. For children 9 to 12 years of age, there were significant and large negative correlations between hyperactivity scores and neuropsychological test scores. Thus, the results indicated that hyperactivity/inattention has an effect on test performance, specifically, the number of digits correctly reversed (Massman et al., 1988).

The results of the current study revealed that the time taken on the Trail Making Test Part B correlated with many other measures of attention, including the WISC-R Digit Span Forward and Backward subtests, and trials A1 and B1 of the RAVLT. Thus, the results of this study imply that the time taken on the Trail Making Test Part B is an adequate indicator of visual divided attention. Additionally, the time taken on the Trail Making Test Part B appeared to indicate how participants will perform on the other aspects of the Trail Making Test. In contrast to this, the results of the current study revealed that the number of errors that participants make on the Trail Making Test Part A does not appear to provide much information, other than to indicate how participants will perform on other aspects of the Trail Making Test. Thus, this measure did not appear to provide a good indication of visual focused attention.

A previous study evaluated the classification accuracy of a commonly used attention/concentration measure, the time taken on the Trail Making Test. Participants included 413 patients who completed a comprehensive neuropsychological evaluation. Classification accuracy of the Trail Making Test Part B ($r = .75$) was acceptable; however, classification accuracy of the Trail Making Test Part A ($r = .62$) was poor. Given that sensitivity rate was not adequate for the Trail Making Test Part A, there remains a need to utilise highly sensitive measures in addition to these embedded measures (Busse & Whiteside, 2012).

During administration of the WISC-R Picture Completion subtest, the examiner shows the subject incomplete pictures of human features, familiar objects, or scenes, with instructions to point out what important part is missing. It was included in the present study as a measure of visual focused attention. This test was found to relate to the time taken on the Trail Making Test Part B, and the number of uncorrected errors on trials 1 and 4 of the Stroop Colour-Word Interference Test, Thus, the WISC-R Picture Completion subtest appeared to measure visual attention.

A previous study investigated some cognitive functions, including attention, in relation to the overall state of monoamine activity in patients with schizophrenia. The neuropsychological battery included the Picture Completion subtest. Profiles of the relations of the activity of dopamine, noradrenaline and serotonin to neuropsychological dysfunction in major patient sub-groups with their very different cognitive characteristics have not been reported. Serum measures of dopamine, noradrenaline and serotonin turnover were examined by regression analyses for the prediction of performance on neuropsychological measures in 108 patients with schizophrenia and 63 matched controls. Paranoid and non-paranoid subgroups were based on ratings from the Positive and Negative Syndrome Scale (PANSS). Right-sided cerebral function, as investigated with the Picture Completion subtest was sensitive to the relative activities of the monoamines: the authors posited that low dopaminergic

activity predicted poor attentional set control in those participants with ideas of reference (Oades et al., 2005).

A factor analytic study of the Wechsler Intelligence Scale for Children – Third Edition (WISC–III) was conducted (Wechsler, 1991). It has been hypothesised that performance on the WISC-III "is greatly facilitated by attention and concentration, whereas it is impaired by distractibility and anxiety" (Kaufman, 1994, p. 209). Specifically, seven year old children were administered the WISC-R Picture Completion subtest. The results of this study suggested that this test was sensitive to attention in school children (Fuentes et al., 2003).

The current study revealed that the number of failures to maintain set on the WCST correlated positively with the WISC-R Digit Span Backward subtest, indicating that as participants were able to correctly reverse longer series of digits, they made more failures to maintain set errors on the WCST. This is a puzzling result, which requires further investigation. The WCST was found to not correlate with any aspect of the Stroop Colour-Word Interference Test. As noted previously, the Stroop Colour-Word Interference Test, especially trial 3, provided a good indication of attention. Thus, the results of this study implied that the number of failures to maintain set on the WCST is an inadequate indicator of visual focused attention.

A previous study examined attention functions in ADHD children using the WCST. The purpose of this study was to explore the relationship between performance on the WCST and cognitive ability. Notably, and in support of the findings of the current study, none of the results of the WCST were found to correlate with attention (Riccio et al., 2009).

Based on the above-mentioned information, it appeared that not all of the neuropsychological measurements behaved as expected when the operational definitions were revisited. This is important to bear in mind when considering the generalisability of the findings of this research. It appears that a more in-depth psychometric study is necessary in order to further examine this particular context and the potential use of these tests.

Lastly, the current research study examined the effects of the clinical variations of the HIV-positive participants on cognitive functioning. It was important to examine the clinical variations of the HIV-positive participants, such as the age at which Highly Active Anti-Retroviral Therapy (HAART) was commenced; the duration of ARV treatment; the World Health Organisation (WHO) stage at diagnosis; the starting and current $CD4^+$ counts; and the starting and current viral loads, when performing neuropsychological examinations, as this provided an understanding of the impact of HIV on attention and concentration functioning.

In the current study, the HIV-positive participants were widely distributed regarding these clinical variations. The results indicated that all of these clinical variations impacted significantly on test performance. Thus, one cannot merely group all HIV-positive individuals together when examining neuropsychological test performance, as these factors all played a substantial role in the results.

A previous study examined the association between participants' recent trends in $CD4^+$ and viral loads and cognitive test performance. Eighty three (83) HIV-infected patients with a mean $CD4^+$ count of 428 copies/mm^3 were examined. The authors investigated the relationships between $CD4^+$ cell counts, one-year trends in immunologic function, and cognitive performance. One-year clinical history for $CD4^+$ cell counts was predictive of attention difficulties. Models that combined recent clinical history trends and $CD4^+$ cell counts suggested that recent clinical trends were more important in predicting current cognitive performance. This research suggested that recent $CD4^+$ and viral load history is an important predictor of current cognitive function across several cognitive domains, including attention and concentration (Tate et al., 2011).

Another study hypothesised that performance on measures of attention, including the Trail Making Test Parts A and B, and the Stroop Colour-Word Interference Test, would be affected by HIV clinical variables such as $CD4^+$ and HIV ribonucleic acid (RNA) levels, duration of illness, anti-retroviral treatment and plasma cytokine concentrations. Performance on the neurocognitive measures was found to be associated with cytokine concentrations; cytokine concentrations were amongst the strongest predictors of neurocognitive function relative to other clinical factors. The authors argued that their findings also pointed to the potential value of simultaneously examining a panel of different biomarkers as a complex relationship likely exists amongst cytokines and that these relationships are mediated not only by HIV infection but also by anti-retroviral treatment and other comorbid conditions (Cohen et al., 2011).

Consistent with these studies, the results of the current study indicated that the clinical variations, such as the age at which HAART was commenced; the duration of ARV treatment; the WHO stage at diagnosis; the starting and current $CD4^+$ counts; the starting viral load; and the current viral load, impact significantly on test performance.

A previous study by Wiley et al. (1998) noted that there is some controversy regarding the importance of viral load in mediating neurologic disease and its effects on cognition, including attention. Nevertheless, the current viral load was found to be important in that study. The authors used RNA assays to examine the HIV viral load in the plasma and the cerebrospinal fluid (CSF) in brains from ten autopsied HIV-infected subjects and two non-infected controls. HIV was found not to be

uniformly distributed throughout the brain. Selective regions, including the basal ganglia and the hippocampus, showed higher levels of virus than the cerebellar cortex and mid-frontal cortical gray matter. The authors held that disruption of these subcortical structures, and the subsequent impact on the subcortical-cortical pathways, would lead to difficulties in attention.

Singh (2009) notes that neurocognitive impairment, including attention and concentration deficits, occurs in 10 – 60 percent of people living with HIV/AIDS, depending on the stage of the disease. $CD4^+$ cell counts in HIV-negative individuals are normally between 500 and 1,600 cells/mm3 (AVERT, 2011). The HIV-positive participants in the current research had a mean $CD4^+$ cell count of 625.82, which is within the normal range, and would indicate that they were in WHO Stages 1 and 2.

Previous literature has argued that the characteristic neuropsychological symptomatology of HIV-infected adults includes higher-order attentional disturbance (Hardy & Hinhn, 2002). Additionally, attentional functioning has been investigated and found to be worse in HIV-positive than HIV-negative children (Watkins et al., 2000). Specifically, HIV-infected children have been found to show deficits in divided-attention activities (Hinkin et al., 2000). Another study that was conducted on adolescents where attentional functioning was examined in HIV-positive and HIV-negative participants found that there was a decrement in attention in the HIV-positive group that was not present in the HIV-negative group (Watkins et al., 2000). Thus, HIV appears to affect attentional functioning in adult, children and adolescents. In line with these research findings, the current study indicated that verbal and visual focused, as well as verbal and visual divided attention, are negatively affected in HIV-positive adolescents.

The benefit of starting ARV treatment for people with minor neurocognitive disorder, including difficulties with attention and concentration, is currently inconclusive (Singh, 2009). In the current study, the HIV-positive participants had been on HAART for an average of 6.15 years, which was almost half of these participants' life-spans. Furthermore, they were placed on HAART only after becoming symptomatic, in keeping with policy rulings in South Africa prior to 2004/5 that prevented the rollout of ARV treatment in the public sector (Butler, 2005). That their verbal and visual focused attention, as well as their verbal and visual divided attention was overall not significantly different from the HIV-negative sample implies that there is a benefit to starting ARV treatment for people with minor neurocognitive disorder. Fortunately, South African policy decisions have changed and ARVs are now being provided in the public sector. The current research indicates a beneficial impact on attention and concentration functions with HIV-positive individuals being on HAART.

11. Limitations of the Study and Suggestions for Future Research

- Sample characteristics: There were challenges in operationalising the independent variable of HIV status in the HIV-negative sample. It was not possible to definitively ascertain if the participants were HIV-negative, due to methodological and ethical issues around questioning this directly. Furthermore, the participants may have been HIV-positive but in the Window Period, and thus, were incorrectly allocated to the HIV-negative sample. This threat to external validity may have affected the relationship that the current study attempted to examine. The researcher recommends that in future research, and bearing ethical considerations in mind, alternate methods be followed to select adolescents that have been definitively diagnosed as HIV-negative on the basis of blood tests.
- Sample characteristics: Medical history, including the frequency that participants became sick, the presence of concomitant illnesses or other premorbid diseases, such as central nervous system diseases, psychoactive medications, substance abuse, systemic illnesses, and psychiatric conditions, can severely affect performance. The current study did not control these extraneous variables, and future research should examine performance in relation to the effects of these factors.
- Sample characteristics: Internal factors that influence neuropsychological test performance include personality traits and mood. These factors were not controlled for in this research. Future research should examine these factors.
- Sample characteristics: Gender was not controlled: both males and females were included in this study, but the genders may not necessarily perform equivalently on neuropsychological tests. Future research should examine the effects of gender in this regard.
- Sample characteristics: The sample size of the current study was small. This reduces the confidence one can place on the generalisability of the results. It is recommended that future studies increase the size of the samples.
- Sample characteristics: The current samples were obtained from specific places; the HIV-positive sample was obtained from the Empilweni Clinic and the HIV-negative sample was obtained from a Sowetan secondary school. This reduces the confidence one can place on the generalisability of the results for the rest of the country. Future studies should sample participants from different places, so as to allow for more generalisable conclusions to be drawn.
- Selection bias: The sample did not accurately reflect the South African population. This may lead to less confidence in the generalisability of the results of the current study. New HIV-positive and HIV-negative samples and sampling techniques should be utilised in future research studies, so as to decrease selection bias.

- Setting: The administration procedure and inter-examiner variability were further threats. It is recommended that future research studies should use one administrator so as to control for the effects of rapport, test administration and scoring.
- Setting: There were discrepancies in the environment in which testing took place between the HIV-positive and HIV-negative samples. Variability in the context of assessment might have had a differential impact on the performance of each activity, which could increase the variance in the scores due to extraneous variables. Future research studies should standardise the setting in which testing takes place.
- Testing: The current study did not control for novelty effects of the participants in relation to the tests; the participants may have been assessed on prior occasions in other settings. This would affect the results obtained in the current study. It is recommended that future studies specifically question whether the participants have been assessed previously and if so, they should not be included in the sample.
- Testing: The current study operationalised attention and concentration based on the performance of the participants on specific tests. In order to either support or disconfirm the results of this study, it is recommended that this study be replicated, measuring the same constructs, but making use of different assessment tools and/or tests.
- Stimulus Characteristics: The neuropsychological tests were developed in foreign contexts, which can affect the psychometric qualities, including the construct validity, reliability, and ecological validity, of the tools when used in South Africa. Thus, the psychometric characteristics of the tests should be explored further before using them again in this context.
- Reactivity of Experimental Arrangements: The results obtained on the neuropsychological tests may have been affected by the fact that the participants were aware that they were being studied. Bearing ethical considerations in mind, future studies should attempt to compare findings on the tests when participants are aware they are being studied, as well as when they are unaware of this.

It is important to note that despite the above-mentioned limitations, the current research study adds value to current literature and knowledge base by expanding research on the attention and concentration functions in samples of HIV-positive and HIV-negative Black, South African adolescents.

12. Conclusions

The current research set out to answer the question as to what the characteristics of attention and concentration are in a sample of Human Immunodeficiency (HIV)-positive adolescents, who were commenced on managed anti-retroviral (ARV) programmes following diagnosis of HIV and immune compromise, in comparison with an equivalent sample of HIV-negative adolescents. The current study also set out to describe the attention and concentration functions of adolescents with HIV on managed ARV programmes; and to compare group differences of attention and concentration functions between adolescents with HIV, who were commenced on managed ARV programmes following diagnosis of HIV and immune compromise, and a contrast group of HIV-negative adolescents. Additionally, it was deemed important to understand how the neuropsychological tests, that were utilised in this study that were assumed to measure attention, behaved in terms of their core function; to elucidate whether the tests that theoretically measure the same function were actually correlated. Lastly, it was deemed important to examine the clinical variations of the HIV-positive participants, such as the age at which Highly Active Anti-Retroviral Therapy (HAART) was commenced; the duration of ARV treatment; the World Health Organisation (WHO) stage at diagnosis; the starting and current $CD4^+$ counts; and the starting and current viral loads, when performing neuropsychological examinations. The following conclusions are made:

- The time taken, the number of uncorrected errors and the number of self-corrected errors on trial 1; as well as the number of uncorrected errors made on trials 2, 3 and 4; and the number of self-corrected errors made on trials 2 and 3 of the Stroop Colour-Word Interference Test were all significantly worse in the HIV-positive participants than in the HIV-negative participants, indicating worse verbal focused attention in the former group.
- The HIV-positive participants made a significantly higher number of errors on the Trail Making Test Parts A and B than did the HIV-negative participants, indicating worse visual focused and divided attention in the HIV-positive individuals.
- The HIV-positive participants completed the Trail Making Test Part A and the WISC-R Coding subtest significantly slower than did the HIV-negative participants, indicating worse visual focused in the HIV-positive individuals.
- The HIV-positive individuals recalled significantly fewer words on trial B1 of the RAVLT than did the HIV-negative participants, indicating worse verbal focused attention in the HIV-positive individuals.
- Tests assessing verbal divided attention were not significantly different in the two samples.
- Trial A1 of the Rey Auditory Verbal Learning Test (RAVLT) correlated with only some of the other measures of attention utilised in this study, whilst trial B1 of the RAVLT correlated with

many of the other measures of attention. Both Trials A1 and B1 of the RAVLT are assumed to assess verbal focused attention, however, trial B1 has a proactive interference effect. It was found that trial B1 appeared to be a better measure of verbal focused attention than trial A1; prior learning seems to make trial B1 load more than trial A1 in this regard.

- The Wechsler Intelligence Scale for Children – Revised (WISC-R) Digit Span Forward subtest was found to be related to the time taken on trials 1, 2 and 4, the number of self-corrected errors on trial 2, and the number of uncorrected errors on trial 4 of the Stroop Colour-Word Interference Test, as well as trial A1 of the RAVLT. Thus, these measures provided good indications of active verbal focused attention.
- The time taken on trial 4 of the Stroop Colour-Word Interference Test was found to relate with many other tests; these measures appeared to be measuring the same construct of verbal focused attention.
- The WISC-R Digit Span Backward subtest was shown to correlate with the time taken on the Trail Making Test Part B. This indicates that these measures were adequate indicators of divided attention.
- The time taken on the Trail Making Test Part B correlated with many other measures of attention, including WISC-R Digit Span Forward and Backward phases, and trials A1 and B1 of the RAVLT. Thus, the results of this study implied that the time taken on the Trail Making Test Part B was an adequate indicator of visual divided attention.
- The number of errors that the participants made on the Trail Making Test Part A did not appear to provide much information, other than to indicate how participants would perform on other aspects of the Trail Making Test. Thus, this measure did not appear to provide a good indication of visual focused attention.
- The WCST was not found to correlate with any aspect of the Stroop Colour-Word Interference Test. As noted previously, the Stroop Colour-Word Interference Test, especially trial 1, provided a good indication of attention. Thus, the number of failures to maintain set on the WCST was an inadequate indicator of visual focused attention.
- All of the clinical variations of the HIV-positive participants, including the age at which HAART was commenced; the duration of ARV treatment; the WHO stage at diagnosis; the starting and current $CD4^{+}$ counts; the starting viral load; and the current viral load, impacted significantly on test performance. Thus, one cannot merely group all HIV-positive individuals together when examining neuropsychological test performance, as these factors played a substantial role in the results.

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14. Appendices

14.1 Appendix 1. Biographical Information Questionnaire

BIOGRAPHICAL QUESTIONNAIRE

Collateral/Home Information

I am going to ask you some questions about the home and family

1. Where does your child live? .....

2. Can you talk about the type and number of rooms in the house?

	Yes	**No**
Bedroom?	1	0
If yes, how many?		
Bathroom?	1	0
Kitchen?	1	0
Living room?	1	0

3. Who lives at home with the child?

	Yes	**No**	
Mother?	1	0	
Father?	1	0	
Grandmother?	1	0	
Grandfather?	1	0	
Mother's boyfriend?	1	0	
Father's girlfriend?	1	0	
Brothers?	1	0	How many?
Sisters?	1	0	How many?
Aunts?	1	0	How many?
Uncles?	1	0	How many?
Other?			

4. Who is the person that takes care of your child most of the time?

Mother	1
Father	2
Grandmother	3
Grandfather	4
Aunt	5

Uncle	6
Sister	7
Brother	8
Mother's boyfriend	9
Father's girlfriend	10
Other	11……

5. Do the parents or guardians work?

Yes	**No**	**If Yes: What kind of work do they do?**
1	0	
1	0	
1	0	

	Yes	**No**	**Don't know**
Have at least one of the parents/guardians passed grade 8?	1	2	3
Are there more than 20 hard-cover books in the home?	1	2	3
Does at least one of the parents/guardians read a newspaper or magazine once a week?	1	2	3
Does the child usually receive a present from their parents/guardians on their birthday?	1	2	3
Is the attitude of the parents/guardians towards schooling positive or at least neutral?	1	2	3
Is there enough money at home for basic things like food, clothes?	1	2	3
Is there enough money to buy expensive things? (e.g. plasma TV)	1	2	3

Is there:	**Yes**	**No**
A TV that is working at home?	1	0
A radio that is working at home?	1	0
A hot water tap inside your home?	1	0
A flush toilet?	1	0
A parent/guardian who has their own car?	1	0
A vegetable garden at home?	1	0
Electricity in the home?	1	0

Gas at home?	1	0
A fridge at home?	1	0
A bed that the child sleeps on by himself/herself?	1	0
A bedroom that the child sleeps in?	1	0
If not, in what room does he/she sleep in?		
Is your child sleeping alone in the bedroom?	1	0
If not, who do you share it with?		

Does the child eat:	**Yes**	**No**	**What does he/she usually eat?**
Breakfast?	1	0	
Lunch?	1	0	
Dinner?	1	0	

	Yes	**No**	**Don't know**
Did the mother have any problems during her pregnancy with the child?	1	2	3
Were there any problems during the birth?	1	2	3
Did the child learn to walk, talk etc. at around the right age?	1	2	3
Comments			

Has the child ever received:	**Yes**	**No**	**If so, when and for what?**
Psychotherapy?	1	0	
Physiotherapy?	1	0	
Occupational therapy?	1	0	
Speech therapy?	1	0	
Had your eyes tested?	1	0	
Had any other forms of treatment?	1	0	
If so, what?			

Could you tell me about the languages spoken at home?

6. Language Context Information

Languages Used	**Home**	**School**	**Friends**	**Mom**	**Dad**	**Grand-parents**

English						
Afrikaans						
Zulu						
Sesotho						
Xhosa						
(Tshivenda) Venda						
(Setswana) Tswana						
Siswati						
Ndebele						
(Xitsonga) Tsonga						
(Sepedi) N. Sotho						

PARTICIPANT QUESTIONS:

I need some background information before we start. I am going to ask some questions about you starting with the languages you speak

1. Participant languages:

Languages	**Read**	**Write**	**Speak**
English			
Afrikaans			
Zulu			
Sesotho			
Xhosa			
(Tshivenda) Venda			
(Setswana) Tswana			
Siswati			
Ndebele			
(Xitsonga) Tsonga			
(Sepedi) Northern Sotho			

I'm going to ask you some questions about your school

2. What language do you learn in at school? ……. (Should be English but check)

3. What grade are you currently in? ……

4. Have you ever repeated a grade at school?

Yes	**No**

1	0
Which Grade?	

5. Have you been absent from school this year?

Yes	**No**
1	0
Why?	

6. What do you do straight after school? ……

……

7. What do you do when you get home from school? ……..

……

	Yes	**No**	**Don't know**
Do you smoke?	1	2	
Do you drink alcohol?	1	2	
If so, how much in a week?			
Do you take drugs?	1	2	
If so, how often and what?			
Do you exercise regularly?	1	2	
Are you in a relationship?	1	2	

Now I'm going to ask some questions about which hand you use to do things

Which hand do you use…?	**Left**	**Right**	**Both**	**Not sure**
To write a letter legibly				
To throw a ball				
To cut with scissors				
To deal playing cards				
To hammer a nail into wood				
To turn a door handle				
To unscrew a jar				
To hold your toothbrush				
Which foot do you use…?				
To kick a ball				
To step on a bug				
Which eye do you use…?				
To look through a vuvuzela				
To look through a hole				

Clinical Impressions: ……..…

14.2 Appendix 2: Human Research Ethics Committee (Medical) Approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Miss Kelly Holland

CLEARANCE CERTIFICATE	**M120268**
PROJECT	Neuropsychological Profile of HIV Positive Adolescents on Anti-retroviral Treatment in Johannesburg, South Africa
INVESTIGATORS	Miss Kelly Holland .
DEPARTMENT	Department of Psychology
DATE CONSIDERED	24/02/2012
+DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 20/04/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : E Schutte et al

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

14.3 Appendix 3: Consent Form from the Empilweni Clinic at the Rahima Moosa Mother and Child Hospital

Empilweni Services and Research Unit
Rahima Moosa Mother and Child Hospital, JHB

South Africa (Private Bag X20 Newclare 2112) • Tel: +27(0)11 470 9290 / 9105
Fax: +27(0)11 673 4905 • E-mail: Ashraf.Coovadia@wits.ac.za

6 February 2012

To whom It May Concern:

Re: Neuropsychological research on HIV positive adolescents attending the Empilweni Clinic

Ms Urvashi Chiba, Mr Daniel Greenslade, Ms Shona Fraser, Ms Stephanie MacIlwaine, Ms Kelly Holland

This letter serves to confirm that, I, Professor Ashraf Coovadia, support the study conducted by the above-mentioned MA (Neuropsychology) students.

In my capacity as head of the Wits Empilweni Clinic; access to the database of patients attending the Empilweni Clinic is granted with permission to conduct the neuropsychological research assessments on willing participants.

Yours faithfully

Professor Ashraf Coovadia
Head of HIV services and Director of ESRU
Rahima Moosa Mother and Child Hospital

14.4 Appendix 4: Permission from the Rahima Moosa Mother and Child Hospital Psychiatry/Psychology Department

Dear Urvash,

I have read your request and would be happy to assist with rooms for your assessment, pending ethics approval and approval from our CEO Mrs. S. Jordaan who I have included on the email.

We can offer you our family therapy room and two offices, as well as the chairs and desks you require.

My only request is that the patients recruited are dealt with directly by you and your team and will not interfere with the running of our clinic or interrupt our staff members.

Regards,

Salisha Maharaj

Clinical Psychologist

Rahima Moosa Hospital

Department of Psychology and Psychiatry

T:

C:

Salisha.Maharaj@gauteng.gov.za

14.5 Appendix 5: Gauteng Department of Education Research Approval Letter

education
Department: Education
GAUTENG PROVINCE

For administrative use:
Reference no. D2012/235

GDE RESEARCH APPROVAL LETTER

Date:	**15 March 2012**
Validity of research Approval:	**15 March 2012 to 30 September 2012**
Name of Researcher:	**Holland K.**
Address of Researcher:	**2 Gardenia Road**
	Primrose
	Germiston
	1401
Telephone Number:	**011 021 6112 / 083 449 6416**
Email address:	**kelly.holland149@gmail.com**
Research Topic:	**Neurophysical profile of HIV positive adolescents on antiretroviral treatment in Johannesburg**
Number and type of schools:	**THREE Secondary Schools**
District/s/HO	**Johannesburg South**

Re: Approval in Respect of Request to Conduct Research

This letter serves to indicate that approval is hereby granted to the above-mentioned researcher to proceed with research in respect of the study indicated above. The onus rests with the researcher to negotiate appropriate and relevant time schedules with the school/s and/or offices involved to conduct the research. A separate copy of this letter must be presented to both the School (both Principal and SGB) and the District/Head Office Senior Manager confirming that permission has been granted for the research to be conducted.

The following conditions apply to GDE research. The researcher may proceed with the above study subject to the conditions listed below being met. Approval may be withdrawn should any of the conditions listed below be flouted:

1. *The District/Head Office Senior Manager/s concerned must be presented with a copy of this letter that would indicate that the said researcher/s has/have been granted permission from the Gauteng Department of Education to conduct the research study.*
2. *The District/Head Office Senior Manager/s must be approached separately, and in writing, for permission to involve District/Head Office Officials in the project.*

1

Making education a societal priority

Office of the Director: Knowledge Management and Research
9th Floor, 111 Commissioner Street, Johannesburg, 2001
P.O. Box 7710, Johannesburg, 2000 Tel: (011) 355 0506
Email: David.Makhado@gauteng.gov.za
Website: www.education.gpg.gov.za

14.6 Appendix 6: Parental Information Sheet (Contrast group)

School of Human and Community Development
Private Bag 3, Wits 2050, Johannesburg, South Africa
Tel: 27 (0)11 717 4524/5; Fax: 27 (0)11 717 4556

Dear Parent/Guardian,

Our names are Daniel Greenslade, Urvashi Maganlal (née Chiba), Shona Fraser, Stephanie MacIlwaine, Jessica Rice (née Fry), Cindy van Wyk, and Kelly Holland. We are conducting research for the purpose of obtaining a Masters degree (MA[Neuropsychology]) at the University of the Witwatersrand. Our area of focus is young adolescents.

We would like to invite your child to take part in this study.

If you, as the guardian/parent agree to allow your child to participate, they will be required to complete some neuropsychological tests which include drawing tasks, repeat some lists of words and numbers, and identify some colours. This may take between four to five hours to complete with rests in between. Your child will be provided with light refreshments half-way through the tests.

Participation is voluntary, and no individual will be advantaged or disadvantaged in any way for choosing to, or not to, participate. Please be assured that confidentiality about the results between the researcher and your child as the participant is guaranteed. The information from the test will be coded and names will not be assigned to the information. Your names will not be on any of your information from the study. The information we receive from the tests will only be seen by us and our research supervisors. No individual feedback will be given. This grouped data may be used in publications or conference presentations, but no data that identifies you will be used. Please note that you will be free to stop the procedure at any time and no negative consequences will follow. Your child's participation would be greatly appreciated; the information your child provides will be kept confidential for a period of two (2) years following the completion of the project.

Should you have any further questions, please feel free to contact any of us, or our supervisors at the below mentioned telephone numbers and we will be happy to assist.

This research project will be approved by the ethics committee at the University of the Witwatersrand and if you have any questions you may also contact them.

Thank You and Kind Regards,

Daniel Greenslade 0835605017, Urvashi Maganlal (née Chiba) 0829049867, Shona Fraser 0827468865, Stephanie MacIlwaine 0844449917, Jessica Rice (née Fry) 0823762980, Cindy van Wyk 0722797828, Kelly Holland 0834496416

Project Coordinator: Enid Schutte
Supervisors: Kate Cockcroft, Aline Ferreira Correia, Marilyn Lucas

14.7 Appendix 7: Parental Consent Form (Contrast Group)



UNIVERISTY
OF THE
WITWATERSRAND,
JOHANNESBURG

School of Human and Community Development
Private Bag 3, Wits, 2050, Johannesburg, South Africa
Tel: (011) 717 4500; Fax: (011) 717 4559

I, Mother/Father/Legal Guardian of_____, give consent for my child to participate in this study

I understand that:

- There is no risk or harm that could come to my child from taking part;
- Participation is voluntary;
- My child, or I, may choose to stop the testing at any time, for any reason, with no penalty;
- My child's results will remain confidential; and
- No positive or negative consequences will follow from choosing to, or not to, participate.

By allowing my child to participate I state that:

- My child has no history of epilepsy, meningitis, HIV infection, neurocognitive impairment, serious head injury, nor are they taking chronic medication or live outside a nuclear family unit; and
- All the relevant information about this research has been explained to me and my child, clearly and simply, and I understand the information;

Signed: _____ Date: _____

Assigned Participant Number: _____

14.8 Appendix 8: Participant Assent Form (Experimental group)



UNIVERISTY
OF THE
WITWATERSRAND,
JOHANNESBURG

School of Human and Community Development
Private Bag 3, Wits, 2050, Johannesburg, South Africa
Tel: (011) 717 4500 Fax: (011) 717 4559

Hello,

We (Kelly Holland, Daniel Greenslade, Shona Fraser, Stephanie MacIlwaine, Jessica Rice [née Fry], Cindy van Wyk and Urvashi Maganlal [née Chiba]) are all students at Witwatersrand University and we are doing a study on adolescents attending the Empilweni Clinic for treatment. We would like you to take part in the study. If you agree to join in, you will be required to complete some drawing tasks, repeat some lists of words and numbers, identify some colours as well as try your hand with some cards.

If you are happy to take part we would like your written permission. If you decide not to, that is okay and no one will be upset. If you decide to join and then later change your mind and want to stop, this is okay too.

Would you like to participate (*Tick **one** box?*)

☐ Yes, I am willing

☐ No, I do not want to

Signing at the bottom of this form means that you agree to take part in this research.

Thank you very much.

Signed (You can just write your name): _____

Date: _____

Assigned Participant Number: _____

14.9 Appendix 9: Parental Consent Form (Experimental Group)



UNIVERISTY
OF THE
WITWATERSRAND,
JOHANNESBURG

School of Human and Community Development
Private Bag 3, Wits 2050, Johannesburg, South Africa
Tel: (011) 717-4500; Fax: (011) 717-4559

I, Mother/Father/Legal Guardian of

_____, give consent for my child to participate in this study.

I understand that:

- There is no risk or harm that could come to my child from taking part;
- Participation is voluntary;
- My child, or I, may choose to stop the testing at any time, for any reason, with no penalty or loss of benefits;
- My child's results will remain confidential; and
- No positive or negative consequences will follow from choosing to, or not to, participate.

By allowing my child to participate, I state that:

- My child has no history of epilepsy, meningitis, or serious head injury;
- All the relevant information about this research has been explained to me and my child, clearly and simply, and I understand the information; and
- The researchers have access to my child's file at the clinic in order to get the demographical and medical information they require.

Signed: _____ Date: _____

Assigned Participant Number: _____

14.10 Appendix 10. Participant Selection Form

To be completed by Case Manager/Doctor
(Only if all boxes ticked, proceed to details below)

Criteria for inclusion	
Age 13.0 up to but less than 16 years	
Vertically acquired	
First Line HAART	
No TBI, Meningitis or co-morbid conditions such as Downs Syndrome, Autism, Epilepsy *(* Note HIV **not** excluded)*	
Non-institutionalised (in family-type setting)	
Minimum of 4 years of schooling in English medium (includes repeated grades)	

Date…… Code……..
1. Gender: Male [1] Female [2]
2. D.O.B: …….
3. Age: ……. (To confirm D.O.B)
4. Home Language: Sotho [1] Zulu [2] Xhosa [3] English [4] Afrikaans [5] Other [6]

5.	Age at which HAART initiated	
6.	WHO stage of HIV at diagnosis	
7.	$CD4^+$ count at time of HAART initiation	
8.	Viral load at time of HAART initiation	
9.	Current $CD4^+$ Count	
10.	Current Viral Load	
11.	Any other chronic medication (e.g. Ritalin etc.)	

Thank you for your help

14.11 Appendix 11: Parental Information Sheet (Experimental group)

School of Human and Community Development
Private Bag 3, Wits 2050, Johannesburg, South Africa
Tel: 27 (0)11 717 4524/5; Fax: 27 (0)11 717 4556

Dear Parent/Guardian,

Our names are Daniel Greenslade, Urvashi Maganlal (née Chiba), Shona Fraser, Stephanie MacIlwaine, Jessica Rice (née Fry), Cindy van Wyk and Kelly Holland. We are conducting research for the purpose of obtaining a Masters degree (MA[Neuropsychology]) at the University of the Witwatersrand. Our area of focus is young adolescents attending the Empilweni Clinic for treatment.

We would like to invite your child to take part in this study.

If, as the guardian/parent, you agree to allow your child to participate, they will be required to complete some neuropsychological tests which include some drawing tasks, repeat some lists of words and numbers, and identify some colours. This may take between four to five hours to complete with rests in between. Your child will be provided with light refreshments half-way through the tests.

Participation is voluntary, and no individual will be advantaged or disadvantaged in any way for choosing to, or not to, participate. Please be assured that confidentiality about the results between the researcher and your child as the participant is guaranteed. The information from the test will be coded and names will not be assigned to the information. The information we receive from the tests will only be seen by us and our research supervisors. No individual feedback can be given as the participants are on a managed treatment programme, therefore, test results will be supplied to the medical practitioner to be used at their discretion. This grouped data may be used in publications or conference presentations, but no data that identifies your child will be used. Please note that you will be free to stop the procedure at any time and no negative consequences will follow. Your child's participation would be greatly appreciated; the information your child provides will be kept confidential for a period of two (2) years following the completion of the project.

Should you have any further questions, please feel free to contact any of us, or our supervisors at the below mentioned telephone numbers and we will be happy to assist.

This research project will be approved by the ethics committee at the University of the Witwatersrand and if you have any questions you may also contact them.

Thank You and Kind Regards,

Daniel Greenslade 0835605017, Urvashi Maganlal (née Chiba) 0829049867, Shona Fraser 0827468865, Stephanie MacIlwaine 0844449917, Jessica Rice (née Fry) 0823762980, Cindy van Wyk 0722797828, Kelly Holland 0834496416

Project Coordinator: Enid Schutte
Supervisors: Kate Cockcroft, Aline Ferreira Correia, Marilyn Lucas

14.12 Appendix 12: Participant Information Sheet (Experimental Group)

School of Human and Community Development
Private Bag 3, Wits 2050, Johannesburg, South Africa
Tel: 27 (0)11 717 4524/5; Fax: 27 (0)11 717 4556

Hello!

Our names are Daniel Greenslade, Maganlal (née Chiba), Shona Fraser, Stephanie MacIlwaine, Jessica Rice (née Fry), Cindy van Wyk and Kelly Holland. We are conducting research for the purpose of obtaining a Masters degree (MA[Neuropsychology]) at the University of the Witwatersrand. Our area of focus is young adolescents attending the Empilweni Clinic.

We would like to invite you to take part in this study.

Your parents have to give consent to let you be part of the study and you will also need to give us assent (your permission) to participate in the study.

You will be required to complete some drawing tasks, repeat some lists of words and numbers, and identify some colours. This may take between four to five hours to complete with rests in between. You will be provided with light refreshments half-way through the tests.

Participation is voluntary, and you will not be advantaged or disadvantaged in any way for choosing to, or not to, participate. Please be assured that confidentiality about the results between the researcher and you as a participant is guaranteed. Your name will not be on any of your information from the study. The information we receive from the tests will only be seen by us and our research supervisors. No individual feedback can be given. This grouped data may be used in publications or conference presentations, but no data that identifies you will be used. Please note that you will be free to stop the procedure at any time and no negative consequences will follow. Your participation would be greatly appreciated; the information you provide will be kept confidential for a period of two (2) years following the completion of the project.

Should you have any further questions, please feel free to contact any of us, or our supervisors at the above mentioned telephone numbers and we will be happy to assist.

This research project will be approved by the ethics committee at the University of the Witwatersrand and if you have any questions you may also contact them.

Thank You and Kind Regards,

Daniel Greenslade 0835605017, Urvashi Maganlal (née Chiba) 0829049867, Shona Fraser 0827468865, 99Stephanie MacIlwaine 0844449917, Jessica Rice (née Fry) 0823762980, Cindy van Wyk 0722797828, Kelly Holland 0834496416

Project Coordinator: Enid Schutte
Supervisors: Enid Schutte, Kate Cockcroft, Aline Ferreira Correia, Marilyn Lucas

14.13 Appendix 13: Reimbursement Letter



UNIVERISTY OF THE WITWATERSRAND, JOHANNESBURG

School of Human and Community Development

Private Bag X3, Wits, 2050, Johannesburg, South Africa

Tel: (011) 717 4500 Fax: (011) 717 4559

Medical Ethics number _____

Hello,

Thank you very much for participating in our research project. This serves as an acknowledgement stating that you received your R50 reimbursement for your travel expenses that you incurred during the participation.

Please sign at the bottom to say you received this reimbursement.

Thank you very much,

Signed (You can just write your name): _____

Date: _____

Researcher's Signature: _____

Assigned Participant Code: _____

14.14 Appendix 14: Participant Information Sheet (Contrast Group)

School of Human and Community Development
Private Bag 3, Wits 2050, Johannesburg, South Africa
Tel: 27 (0)11 717 4524/5; Fax: 27 (0)11 717 4556

Hello!

Our names are Daniel Greenslade, Urvashi Maganlal (née Chiba), Shona Fraser, Stephanie MacIlwaine, Jessica Rice (née Fry), Cindy van Wyk and Kelly Holland. We are conducting research for the purpose of obtaining a Masters degree (MA[Neuropsychology]) at the University of the Witwatersrand. Our area of focus is young adolescents.

We would like to invite you to take part in this study.

If you agree to join in you will be required to complete some drawing tasks, repeat some lists of words and numbers, and identify some colours. This may take between four to five hours to complete with rests in between. You will be provided with light refreshments half-way through the tests.

Participation is voluntary, and you will not be advantaged or disadvantaged in any way for choosing to, or not to, participate. Please be assured that confidentiality about the results between the researcher and you as a participant is guaranteed. The information we receive from the tests will only be seen by us and our research supervisors. No individual feedback can be given. This grouped data may be used in publications or conference presentations, but no data that identifies you will be used.

Please note that you will be free to stop the procedure at any time and no negative consequences will follow. Your participation would be greatly appreciated; the information you provide will be kept confidential for a period of two (2) years following the completion of the project.

Should you have any further questions, please feel free to contact any of us, or our supervisors at the above mentioned telephone numbers and we will be happy to assist.

This research project will be approved by the ethics committee at the University of the Witwatersrand and if you have any questions you may also contact them.

Thank You and Kind Regards,

Daniel Greenslade 0835605017, Urvashi Maganlal (née Chiba) 0829049867, Shona Fraser 0827468865, Stephanie MacIlwaine 0844449917, Jessica Rice (née Fry) 0823762980, Cindy van Wyk 0722797828, Kelly Holland 0834496416

Project Coordinator: Enid Schutte
Supervisors: Enid Schutte, Kate Cockcroft, Aline Ferreira Correia, Marilyn Lucas

14.15 Appendix 15: Participant Assent Form (Contrast group)



UNIVERISTY
OF THE
WITWATERSRAND,
JOHANNESBURG

School of Human and Community Development
Private Bag 3, Wits, 2050, Johannesburg, South Africa
Tel: (011) 717 4500; Fax: (011) 717 4559

Hello,

We (Kelly Holland, Daniel Greenslade, Shona Fraser, Stephanie MacIlwaine, Jessica Rice [nee Fry], Cindy van Wyk and Urvashi Maganlal [nee Chiba]) are all students at Witwatersrand University and we are doing a study on adolescents at your school. We would like you to take part in the study. If you agree to join in you will be required to complete some drawing tasks, repeat some lists of words and numbers, identify some colours as well as try your hand with some cards.

If you are happy to take part we would like your written permission. If you decide not to, that is okay and no one will be upset. If you decide to join and then later change your mind and want to stop, this is okay too.

Would you like to participate (*Tick **one** box?*)

☐ Yes, I am willing

☐ No, I do not want to

Signing at the bottom of this form means that you agree to take part in this research.

Thank you very much.

Signed (You can just write your name): _____

Date: _____

Assigned Participant Number: _____