Executive Functioning in a HIV-positive Paediatric Sample

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Declaration

A research project submitted in partial fulfilment of the requirements for the degree of MA by coursework and research report in the field of Psychology in the Faculty of Humanities, University of the Witwatersrand, Johannesburg, 15 March 2024.

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

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Abstract

High prevalence of Human Immunodeficiency Virus (HIV) poses significant public health challenges in regions like Sub-Saharan Africa, especially among children and adolescents. Despite advancements in reducing vertical mother-to-child transmission and increasing access to antiretroviral therapies, paediatric populations continue to face substantial neurocognitive challenges associated with HIV infection. This study aimed to establish a profile of executive functioning in a South African paediatric population using cognitive measures (the NEPSY-II) and a behavioural rating scale (the BRIEF) to elucidate the cognitive impact of HIV. Assessing executive functions in children presents challenges due to their multifaceted nature, with cognitive measures and behavioural rating scales offering differing insights. As such, a secondary aim of this paper was to examine the inter-correlations between these measures. The participant group was comprised of 40 children living with HIV in Johannesburg, South Africa, aged 10-16. Normative data for comparisons were obtained from the NEPSY-II and BRIEF manuals, as well as a sample of NEPSY-II raw scores for South African youth without a central nervous system disease (Truter et al., 2017). Significant differences were found between the HIV+ group and comparison samples. Specifically, HIV+ children showed poorer performance in working memory, inhibitory control and cognitive flexibility compared to their typically developing peers. These results provide insights into executive function challenges faced by HIV+ children and adolescents, emphasising the importance of early intervention and support.

KEYWORDS: HIV, Paediatric populations, Neurocognitive challenges, Executive Functioning (EF), South African, Cognitive measures, Behavioural rating scale, Cognitive flexibility, Inhibitory Control, Working Memory

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Finally, I dedicate this thesis to my husband, Stuart. Thank you for everything, but most of all for sharing this life with me.

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List of Acronyms

ADHD: Attention Deficit Hyperactivity Disorder

AIDS: Acquired Immunodeficiency Syndrome

ART: Antiretroviral Therapy

ARV: Antiretroviral Drugs

ASD: Autism Spectrum Disorder

ATP: Adenosine Triphosphate

BADS-C: Behaviour Assessment of Dysexecutive Functions for Children

BBB: Blood Brain Barrier

BRI: Behaviour Regulation Index

BRIEF: Behaviour Rating Inventory of Executive Function

cART: Combination Antiretroviral Therapy

CBCL: Child Behaviour Checklist

CEN: Central Executive Network

CFA: Confirmatory Factor Analysis

CIS: Columbia Impairment Scale

CNS: Central Nervous System

DNA: Deoxyribonucleic Acid

EFs: Executive Functions

EFV: Efavirenz

fNIRS: Functional Near-Infrared Spectroscopy

GEC: Global Executive Composite

HAART: Highly Active Antiretroviral Therapy

HAND: HIV Associated Neurocognitive Disorder

HIV: Human Immunodeficiency Virus

HIV-EU: HIV Exposed, Uninfected

HIV-UU: HIV Unexposed, Uninfected

HREC: Humanities Research Ethics Committee

INSTIs: Integrase Strand Transfer Inhibitors

KABC: Kaufman Assessment Battery for Children, First Edition

KABC-II: Kaufman Assessment Battery for Children, Second Edition

LAMIC: Low and Middle Income Countries

MI: Metacognitive Index

MND: Major Neurocognitive Disorders

MPI: Mental Processing Index

MTCT: Mother-to-Child vertical Transmission

NEPSY-II: A Neuropsychological Assessment, Second Edition

NNRTIs: Nonnucleoside Reverse Transcriptase Inhibitors

NVI: Nonverbal Index

OFC: Orbitofrontal Cortex

PFC: Prefrontal Cortex

PHIV: Perinatally Acquired HIV

PIs: Protease Inhibitors

RNA: Ribonucleic Acid

ROS: Reactive Oxygen Species

SA: South African

TBI: Traumatic Brain Injury

USA: United States of America

VABS-II: Vineland Adaptive Behaviour Scale, Second Edition

WCST: Wisconsin Card Sorting Test

WM: Working Memory

Chapter One: Theoretical & Conceptual Review

Introduction and Contextual Review

Human Immunodeficiency Virus (HIV) is a global pandemic with no known cure. According to the United Nations Joint Programme on HIV/AIDS, by the end of 2022 approximately 39.0 million people were living with the virus, with 1.3 million newly reported cases in 2022 alone (UNAIDS, 2023). Globally, South Africa has the highest estimated infection rate of approximately 14%, or 8.5 million people (Stats SA, 2022). With regard to the global population, 1.54 million [1.20 million -2.11 million] children under 15 years old are living with HIV/AIDS, with 130 000 new cases in 2022 (UNAIDS, 2023, UNICEF, 2023). Of this estimated 1.54 million, 87% of children live in sub-Saharan Africa (UNICEF, 2023). Regions of Southern Africa have made significant advancement in reducing the rate of new paediatric infections by 58% since 2010 (UNAIDS, 2023). This is largely due to increased access to education regarding safe infant care and reduction in mother-to-child vertical transmission (MTCT; UNAIDS, 2022). Even though only 4% of individuals living with HIV/AIDS are children, individuals under the age of 15 still account for 10% of new HIV infections and 13% of HIV/AIDS related mortality (UNAIDS, 2023; UNICEF, 2023). In 2022, it is estimated that worldwide approximately 84,000 (56,000 – 120,000) children under the age of 15 succumbed to AIDS-related causes (UNICEF, 2023). This is in part due to children having reduced immunological capacity, combined with existing high rates of MTCT (Ferrand et al., 2009; Lentoor, 2020). Additionally, this population experience a wide range of cognitive and scholastic challenges that impact development and general quality of life (Anabwani et al., 2016). This age group forms the focus of this study, which aimed to understand executive functions of children and adolescents living with HIV in comparison to typically developing peers.

The nosology of HIV distinguishes between two types, HIV-1 and HIV-2, originating from Central African chimpanzees and West African sooty mangabeys, respectively (German Advisory Committee, 2016). While HIV-2 is less infectious and confined mainly to Western and Central Africa, HIV-1 became a global pandemic with various subgroups, including HIV-1 M:C, the most prevalent subtype in Southern Africa (German Advisory Committee, 2016). HIV-1, a type of retrovirus known as a lentivirus, utilises reverse transcriptase enzymes to convert its ribonucleic acid (RNA) into deoxyribonucleic acid (DNA), integrating this 'virus-tainted' DNA into the host's genetic material and ultimately leading to the production of additional infected particles (Poltronieri et al., 2015).

At an immunological level, HIV/AIDS is characterised by a decline in white blood cells known as CD4+T cells (Vidya Vijayan et al., 2017). The CD4 (cluster of differentiation 4) is a glycoprotein that binds to lymphocytes, such as T-cells, producing CD4+T cells that are responsible for assisting the immune system in adaptation and fighting off infection (Leidl et al., 2010). As HIV progresses, the level of CD4+T cells in the body slowly declines, leading to a gradual deterioration of immune function and, if left untreated, eventually death (Vidya Vijayan et al., 2017). Once the CD4+T cell count has dropped below 200 cells/µl in the peripheral blood, the patient is diagnosed with Acquired Immune Deficiency Syndrome (AIDS; Vidya Vijayan et al., 2017). After the CD4+T cell count has declined past 50 cells/µl, patients are at extreme risk of coinfection from pseudomonas pneumonia and tuberculosis, among others (Leidl et al., 2010; Peltzer et al., 2006). The immunological effects of HIV/AIDS are particularly harmful to the paediatric population as an immature CNS and immune system increase virulence of both HIV and possible viral coinfections (Sharer & Cho, 1989). In terms of patient prognosis, CD4 cell count is considered predictive, with higher cell counts indicating better immunological and CNS function (Lentoor, 2020). While management therapies exist, HIV continues to be a leading cause of mortality worldwide. HIV/AIDS related illness accounted for approximately 630 000 deaths in 2022, claiming the lives of 84 000 children (UNAIDS, 2022). Due to poor economic infrastructures, insufficient education, stigma, and high instances of rape and sexual abuse, 260 000 cases of HIV/AID related deaths were individuals living in Sub-Saharan Africa (UNAIDS, 2023).

Currently, the most effective infection management of HIV/AIDS is the use of antiretroviral therapies (ARTs) which act to increase the CD4+T cell count and lower the risk of co-infection (Leidl et al., 2010). These include nonnucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside analogues, integrase strand transfer inhibitors (INSTIs) and protease inhibitors (PIs).The NNRTIs are widely regarded as a staple addition to the combination of therapies used to treat HIV-1 infection (Mackie, 2006). They work by attaching themselves directly to the hydrophobic active site of HIV-1 reverse transcriptase (the enzyme responsible for integrating the infected RNA into DNA in retroviruses) and disrupting its polymerase process (Mackie, 2006). These NNRTIs drugs are often used in a poly-therapeutic treatment approach, as if they are used as monotherapy, resistance develops quickly through mutations in the pol gene (Mackie, 2006). In South Africa, efavirenz (EFV; a type of NNRTI) is a primary antiretroviral drug (ARV) used in paediatric populations (Hammond et al., 2019). However, EFV use in children has been associated with transient neuropsychiatric manifestations, such as drowsiness, seizures, and personality changes (Hammond et al., 2019). While these effects may resolve over time, continued EFV use has raised concerns regarding the impact of EFV toxicity on neurocognition in children living with HIV (Hammond et al., 2019).

Recent research is aimed at developing effective protocols for supplementing ARVs (which seek to reverse HIV proliferation in the CNS) with therapies that reverse HIV viral latency and clear infection to produce a functional cure (Deeks et al., 2021; Margolis et al., 2020). A functional cure for HIV would be one that prevented further infection and eradicated all HIV-associated illnesses without the need for ongoing medication (Margolis et al., 2020). Early intervention allows ARVs to limit uncontrolled HIV reproduction in the brain tissue as quickly as possible, reducing neuroinflammation and damage to the CNS (Winston & Spudich, 2020). As of 2022, 76% of the global population living with HIV had access to ARTs (UNAIDS, 2023). However, only 57% of children under the age of fifteen and 82% of pregnant women living with HIV have been able to access these therapies (UNAIDS, 2023). Germane to my research, while ARVs are effective in reducing the immunological effects of HIV-related illnesses on the CNS, their efficacy to reverse HIV-associated Neurocognitive Disorder (HAND) is diminished ((Boivin et al., 2018; Fairlie et al., 2022; Vazquez-Santiago et al., 2014). As a result, children with HAND may experience a range of neurocognitive difficulties and it is important to understand the nature of these challenges.

While some of these neurocognitive challenges are circumscribed by appropriate medical intervention, milder forms of HAND persist. HIV-Associated Neurocognitive Disorders is a term used to collectively refer to the range of neurocognitive impairments caused by HIV-1 infection (Winston & Spudich, 2020). The current average prevalence of HAND is estimated at 50.41% globally, and 49.57% in Africa (Zenebe et al., 2022). Various psychological, clinical, and socio-demographic variables impact an individual's risk of developing HAND (Zenebe et al., 2022). This is of particular significance as extended exposure to HIV-1 and its associated immune system dysregulation means that individuals who acquire HIV at an early age face an increased likelihood of experiencing neurodevelopmental and neurocognitive deficits later in life compared to those who contract HIV during adulthood (Laughton et al., 2013; N. Phillips et al., 2016; Williams et al., 2021). Moreover, research indicates that these neurocognitive issues persist, even when ART is started as early as 5 months old (Puthanakit et al., 2013; Whitehead et al., 2014).

The neurocognitive effects of HIV, and the pharmacokinetic limitations of ARVs, are of particular importance to paediatric populations, as HIV disrupts the integrity of the fronto-striatal circuit and Central Executive Network (CEN; Britz & van Zyl, 2020; Ipser et al., 2015). The CEN is a vital neural system responsible for the management of higher cognitive functions essential for successful daily functioning (Shen et al., 2020). Comprised of interconnected brain regions, the CEN facilitates executive functions (EFs), a collection of cognitive processes crucial for goal-directed behaviours. Vital nodes within the CEN include the prefrontal cortex, frontopolar cortex, anterior cingulate cortex, and posterior parietal cortex, which collaborate to support various EF tasks such as working memory, inhibition of prepotent responses, attentional control, planning, and cognitive flexibility (Ipser et al., 2015; Shen et al., 2020). Dysfunction within the CEN is associated with deficits in EF observed across a spectrum of neurological and psychiatric conditions, including schizophrenia, Alzheimer's disease and major depressive disorder (Shen et al., 2020).

Executive functions refer to a host of cognitive processes necessary for concentration and attention (Anabwani et al., 2016; Doebel, 2020). Given the various scholastic, social and developmental demands placed on children and adolescents, EFs are particularly important to investigate in atypically developing populations (Anabwani et al., 2016). Research suggests that children living with HIV struggle with academic performance, which could be related to EF difficulties (Cockcroft & Cassimjee, 2020). Currently, education curriculums are established for typically developing children, which places those living with a CNS disease at a scholastic disadvantage (Anabwani et al., 2016). This study investigated how EFs in children and adolescents living with HIV are affected relative to their typically developing peers, in order to better understand the cognitive challenges associated with HIV in paediatric populations.

The following sections provide a comprehensive review of the relevant literature, organised into three broad themes. The first, Paediatric HIV and neurocognitive performance, discusses research pertaining to the neurocognitive effects of HIV in children and adolescents, as well as the cognitive impact of ARVs. The second section examines the role that EFs play in neurocognitive development, academic achievement, and social functioning. Finally, the third section explores the extent to which the relationship between EFs and paediatric HIV has been researched, critically discussing the strengths and weaknesses of these approaches. This review contextualises the topic, ultimately showing how this study adds to the body of literature on EFs in children living with HIV.

Paediatric HIV and Neurocognitive Performance

The HIV virus attacks the nervous system soon after it enters the body, causing a variety of mild to severe physiological and neuropsychological symptoms. Both the peripheral nervous systems and CNS are susceptible to attack from HIV, with the CNS becoming vulnerable to viral infiltration at the earliest stages of infection (McArthur & Smith, 2013). This is due to HIV being transported across the blood-brain barrier (BBB) into the CNS, where it replicates rapidly, inducing chronic infectious virus production (Vazquez-Santiago et al., 2014). The BBB separates the bloodstream from the brain parenchyma and regulates the exchange of molecules between the blood and the CNS, maintaining cerebral homeostasis and protecting the brain from pathogens. This barrier is impermeable to most molecules, including pathogens and therapeutic drugs, due to the presence of tight junction proteins that restrict paracellular passage. It is composed of tightly bound vascular endothelial cells lining the capillaries, along with supportive cells such as astrocytes, which contribute to BBB integrity by ensheathing the capillaries and releasing chemical signals that maintain endothelial cell tightness (Osborne et al., 2020). However, HIV exploits host cells such as macrophages, CD4+ T cells and monocytes, which can cross the BBB, carrying the virus into the CNS in a Trojan horse-like mechanism (Osborne et al., 2020; Vazquez-Santiago et al., 2014).

Chronic viral infections, such as HIV-1, occur when the primary adaptive immune response is unable to remove the initial infection, and so it persists throughout the patient's life, bringing with it a host of systemic, immunological and neurological effects (Vazquez-Santiago et al., 2014). The Trojan horse-like infection strategy not only enables the virus to access the otherwise protected area of the brain, but also contributes to the establishment of viral latent HIV reservoirs within the CNS, posing significant challenges for therapeutic intervention and disease management (Osborne et al., 2020). Latent HIV reservoirs are established soon after the virus enters the body, at the first stage of viral infection (Aiamkitsumrit et al., 2015). Brain imaging and autopsy cerebral analysis on posthumous HIV patients indicate that the frontal lobe is particularity affected as tissue begins to atrophy relatively soon after HIV crosses the BBB (McArthur & Smith, 2013).

Once the virus has infiltrated the CNS, the functional connections within the fronto-striatal circuit become extremely susceptible to infection (Ipser et al., 2015). The *fronto-striatal network* refers to the connection of neural pathways between the striatum (found in the basal ganglia) and the frontal lobe (Morris et al., 2016). This circuit mediates cognitive, emotional and behavioural processes, including EFs such as working memory (WM) as well as focused attention (Morris et al., 2016). The fronto-striatal network is connected to the CEN through cortical networks of catecholamines, particularly dopamine and norepinephrine. HIV-associated neuroinflammation and neurodegeneration deregulate dopaminergic and noradrenergic systems, leading to alterations in neurotransmitter release, receptor sensitivity, and neuronal signalling, which may in turn contribute to cognitive impairments commonly observed in people living with HIV (Nolan & Gaskill, 2019). Additionally, the interplay between catecholamines and the immune system further exacerbates neuroinflammation and neuronal damage, possibly perpetuating this cycle of cognitive decline (Nolan & Gaskill, 2019). As such, dysregulation of the fronto-striatal network often results in impaired EF, especially with regards to WM and verbal fluency (Ipser et al., 2015; Nolan & Gaskill, 2019). Aside from the fronto-striatal circuitry, HIV affects other cerebral regions including the basal ganglia, hippocampus, prefrontal cortex and subcortical white matter (Winston & Spudich, 2020).

HIV associated neurocognitive dysregulation is thought to develop as a response to the immune reaction and inflammation caused by HIV infection of the CNS (Olivier et al., 2018). Specifically, these impairments are thought to manifest due to direct viral effects on the CNS, leading to structural and functional alterations (Fairlie et al., 2022). This is of particular importance to paediatric populations as the impact of the virus on the developing brain during crucial stages of growth and maturation is substantial (Fairlie et al., 2022); thus potentially posing a higher risk for children with HIV to develop neurocognitive challenges compared to adults (Khiati et al., 2010; Williams et al., 2021). Various factors such as sociodemographic and psychosocial variables, neuroinflammation, potential neurotoxic effects of certain ARVs, neuronal injury and, possibly, differences in human host genetics influence an individual's vulnerability to HAND (Dreyer, 2023; Fairlie et al., 2022; Olivier et al., 2018). The pathogenesis and clinical manifestations of HIV in adult patients have been well reported in the literature (Mekuriaw et al., 2023; Olivier et al., 2018). Far less is known regarding the functional and cognitive changes caused by HIV in paediatric patients, although some neuroimaging studies reveal structural abnormalities, such as damage to neural microstructure, reduced grey and white matter volume, ventricle enlargement, cortical atrophy, and basal ganglia abnormalities (Hoare et al., 2014; Phillips et al., 2016; Yadav et al., 2017).

For example, an analysis was conducted on structural connectivity, cortical thickness, subcortical volume and neurocognitive functions in 34 children living with HIV with a mean age of 10.2 years old (*SD = 1.7*) and 32 age and gender-matched healthy controls (Yadav et al., 2017). The study revealed participants living with HIV exhibited significantly different cortical thickness (*p=0.04*) and subcortical volumes (*p=0.032*), indicating potential disruptions in these networks (Yadav et al., 2017). These findings were in line with previous research suggesting similar alterations in grey matter density, cortical thinning, and subcortical atrophy in adolescent and adult HIV patients, which was attributed to HIV viral protein toxicity and inflammatory processes (e.g. Hoare et al., 2012, Cohen et al., 2010a, Cohen et al., 2010b, Sarma et al., 2014, Thompson et al., 2005). The observed changes in paediatric HIV participants may reflect neuronal and glial cell injuries induced by the virus, potentially leading to reduced cortical thickness and subcortical volume (Yadav et al., 2017). These findings emphasise the potential impact of HIV on structural brain alterations and disrupted networks, notably affecting regions involved in memory, sensory interpretation, and cognitive processing (Yadav et al., 2017).

In sub-Saharan Africa, roughly 10% of children (approximately 3.4 million) under the age of 18 are HIV-positive, and despite improved access to cARTs, most will develop some form of HAND (Adams et al., 2019). The next section provides an overview of the current state of knowledge regarding HIV-associated neurocognitive challenges among the paediatric population in Sub-Saharan Africa. Research focused on this region is paramount, as children in sub-Saharan Africa face heightened susceptibility to neurocognitive disorders due to several risk factors associated with limited access to relevant healthcare and lower socio-economic conditions (Fairlie et al., 2022; Musindo et al., 2022).

The neurocognitive functioning of 90 HIV-positive children, aged 8–15 years (m=11.38, SD = 2.06), attending the Comprehensive Care Clinic at Kenyatta National Hospital in Kenya was assessed using the Kaufman Assessment Battery for Children, Second Edition (KABC-II), which has been adapted and validated in Kenya and Uganda (Musindo et al., 2018). Thirteen subtests of the KABC-II were utilised to derive four index scores: (i) sequential processing, measuring working memory; (ii) simultaneous processing, assessing visual-spatial processing and problem-solving abilities; (iii) planning, examining executive reasoning skills; (iv) learning, evaluating immediate and delayed memory; as well as two global scores known as the (i) Mental Processing Index (MPI), a composite score representing key cognitive performance domains, and (ii) Nonverbal Index (NVI), comprising subtests not reliant on language comprehension (Musindo et al., 2018). Notably, the knowledge subtests were not administered due to limited cultural suitability (Boivin et al., 2010). Results revealed significant neurocognitive deficits, with 60% of participants scoring at least two standard deviations below the mean, indicating the presence of major neurocognitive disorders (MND). Specifically, high prevalence of MND was observed in simultaneous processing (62.2%) and planning (63.3%) subscales. However, only 4.4% of participants were found to have significant immunosuppression based on current WHO guidelines, and the majority had low viral loads (<1000 copies per ml), suggesting good adherence to ARVs and viral suppression (Musindo et al., 2018). Interestingly, no significant associations were found between KABC-II subtest performance and viral load, CD4 count, or timing of ART initiation. These findings suggest that despite successful management of HIV with ARTs, children and adolescents living with HIV continue to experience substantial neurocognitive deficits (Musindo et al., 2018).

Similarly, a comprehensive assessment was conducted involving 338 children aged 4–9 years from Cameroon, consisting of three participant groups: HIV positive (n=127), HIV-EU (n=101) and HIV-UU (n=110) groups (Debeaudrap et al., 2018). The study draws on the Pediacam ANRS12140 cohort and employed various assessments. Specifically, neurological function was measured using the Touwen examination, and cognitive function was assessed using the KABC-II, particularly chosen for its perceived cross-cultural validity, especially in African contexts (Debeaudrap et al., 2018). The KABC-II assessment employed seven subtests for children under 6 years and eight subtests for those older than 6 years. These subtests were utilised to generate two global indexes normed on a French population: the nonverbal index (NVI) and the MPI. Additionally, four composite scores were derived, including learning, sequential processing, planning (only for children older than 6 years), and simultaneous processing. The results indicated that children living with HIV exhibited significantly lower unadjusted KABC-II global indexes and scores compared to children in the other groups. For the NVI the HIV+ group (m=56.1, SD =12.6) faired significantly lower (p<0.01) than both the HIV-UE (m= 63.4, SD = 11.8) and HIV-UU (mean = 67.1, SD = 13.2) groups. Similarly, for the MPI, the HIV+ group (m=61.7, SD=14.0) consistently scored significantly lower compared to the HIV-UE (m=73.4, SD=14.7) and HIV-UU (m=78.9, SD=12.8) groups. Even after adjusting for contextual factors, the results highlighted significant differences in neurocognitive performance between HIV-positive children and their uninfected peers, with children living with HIV exhibiting significantly lower KABC-II global indexes and composite scores compared to both HIV-EU and HIV-UU children (Debeaudrap et al., 2018). Additionally, results from the Touwen Examination indicated that the children living with HIV exhibited significantly more neurological dysfunctions and higher levels of behavioural difficulties compared to HIV-UU participants (p = 0.002).

In another study, the relationship between paediatric HIV and neurocognitive development across multiple sub-Saharan African sites was explored by employing a standardised assessment protocol across ten different languages (Boivin et al., 2018). Researchers enrolled 615 children aged 5 to 11 (m=7.2) from the IMPAACT P1060 clinical trial, comparing those with HIV (n=246), HIV-EU (n=183), and HIV-UU (n=182) cohorts (Boivin et al., 2018). Standardised neuropsychological assessments, including the KABC-II and the parent-reported BRIEF were administered. Several subtests from the KABC-II were employed, including sequential processing, simultaneous processing, learning, planning, as well as the NVI and MPI. The HIV-positive cohort demonstrated significantly lower performance particularly on the KABC-II global scales, indicating challenges in sequential processing (WM; p<0.001), planning (p<0.01), and learning (p<0.001) compared to both HIV-EU and HIV-UU groups (Boivin et al., 2018). For the NVI the HIV+ group (m=72.05; 70.61,73.49, 95% CI) faired significantly lower (p<0.001) than both the HIV-UE (m=78.37; 76.68,80.06, 95% CI) and HIV-UU (m=79.02; 77.32,80.72, 95% CI) groups. Similarly, for the MPI, the HIV+ group (m=73.18; 71.86,74.50, 95% CI) consistently scored significantly lower (p<0.001) compared to the HIV-UE (m=79.14 ;77.50,80.78, 95% CI)and HIV-UU (m=80.89 ;79.18, 82.60, 95% CI) groups (Boivin et al., 2018).

In terms of the BRIEF assessment, eight scales were employed, which were further grouped into two overarching indexes: the Behaviour Regulation index (BRI) comprising three scales, and the Metacognition Index (MI) comprising five scales. These scales collectively contributed to the calculation of a Global Executive Composite Score (GEC), where higher scores indicated a greater frequency of day-to-day behavioural problems associated with executive function, as perceived by the parent or caregiver. There were no statistically significant differences between the groups on the BRI (p=0.97), the MI (p=0.07), or the GEC (p=0.34) scales. However, it should be noted that while not statistically significant, there was a tendency for all BRIEF global index GEC scores to be higher for the HIV+ group (m=53.19; 51.51,54.87, 95% CI) compared to the HIV-EU (m=51.52; 49.79,53.26, 95% CI) and the HIV-UU (m=50.55; 49.02,52.08, 95% CI) groups, signifying a higher prevalence of behaviour problems related to executive function among the HIV-positive cohort. These results were consistent across the six study sites, indicating the robustness of the findings. Children living with HIV exhibited significant neuropsychological deficits compared their HIV-UU and HIV-EU peers, despite the HIV+ cohort receiving ARTs from an early age and demonstrating viral suppression and clinical stability at the time of assessment (Boivin et al., 2018). These findings suggest that even with early and consistent medical intervention, children living with HIV in Africa continue to face neurodevelopmental and neurocognitive challenges, emphasising the need for contextually sensitive, African-led research into this area (Laughton et al., 2013; Phillips et al., 2016).

This need for contextually relevant research is reiterated by studies elucidating the functional impact of HIV associated neurocognitive dysfunction on developmental process and overall quality of life (Anabwani et al., 2016; N. Phillips et al., 2022). A study conducted in South Africa among 247 participants aged 9–12 (n=203 HIV+; n=44 HIV-UU control) explored the relationship between cognitive and functional impairment in youth living with HIV (Phillips et al., 2022). In the context of youth living with HIV, functional impairment encompasses challenges adapting to everyday situations, particularly in areas such as interpersonal relationships, academic performance (e.g., school grade repetition), psychopathology, and leisure time utilisation. These challenges indicate underlying cognitive deficits resulting from the viral infection (Phillips et al., 2022). Utilising measures such as the Columbia Impairment Scale (CIS), Child Behaviour Checklist (CBCL), Vineland Adaptive Behaviour Scale – 2nd edition (VABS-II), and school grade repetition as a crude screen for functional impairment, the study highlighted significant associations between cognitive impairment and measures of functional impairment, notably CBCL Total Competence, VABS-II adaptive behaviour composite, and school grade repetition (Phillips et al., 2022). Relative risk ratio analyses revealed that HIV-infected participants diagnosed with neurocognitive disorders were at higher risk for functional impairment across these measures (CIS, CBCL, VABS-II, repeated-grades), emphasising the increased risk of functional impairment in the presence of cognitive deficits (Phillips et al., 2022). However, the study noted limitations such as reliance on self-report measures for functional impairment and the cross-sectional design, underscoring the need for further longitudinal research to establish causal associations and validate screening measures for functional impairment among youth living with HIV in resource-limited settings like South Africa.

The advent of ARVs has marked a pivotal shift in disease management, leading to improved health outcomes and prolonged life expectancy among people living HIV. In the realm of neurocognitive performance, the impact of ARV on cognitive function in paediatric HIV cases remains a subject of ongoing investigation. Studies have shown promising outcomes, indicating that effective ART regimens might mitigate the progression of neurocognitive deficits and potentially ameliorate functional impairment in youth living with HIV (Phillips et al., 2022). However, the debate remains ongoing. This link between ARTs and neurocognitive performance underscores the importance of assessing the efficacy of treatment modalities in addressing not only virological suppression, but also cognitive and functional well-being in paediatric HIV populations. The impact of ARTs on neurocognitive performance will be discussed at greater length in the following section.

Impact of Antiretroviral Therapies on Neurocognitive Performance

Antiretroviral therapy (ART) has revolutionised the management of HIV infection, significantly improving survival rates in both adults and children. In terms of neurocognitive performance, effective ARV use has lessened the severity of HAND but not the frequency (Alford & Vera, 2018). Some research suggests that early initiation of ART can significantly decrease the severity of HIV-related cognitive issues by curbing uncontrolled HIV replication in the brain, reducing inflammation, and preventing damage to the CNS, although milder cognitive problems still persist and impact the lives of those with HIV (e.g. Spudich et al., 2019; Vazquez-Santiago et al., 2014; Winston & Spudich, 2020). Research regarding the potential neuronal toxicity of antiretroviral agents is inconclusive, with mixed clinical evidence indicating both indirect (via vascular processes) and direct (mitochondrial) neurotoxicity mechanisms (Alford & Vera, 2018). Of particular concern to this study, the potential neurotoxic interaction effect could be further impacting on the neurocognitive processes of patients living with HIV (Alford & Vera, 2018; Rubin et al., 2021; Underwood et al., 2015).

Illustrating this is a retrospective study conducted at the Neuro-HIV clinic in the Red Cross War Memorial Children's Hospital in Cape Town, South Africa, which examined the potential neurotoxic effects of EFV-based ARVs on neurocognitive functioning in 12 children living with HIV aged 3–12 years old (Hammond et al., 2019). All participants presented with suspected EFV neurotoxicity, showcasing varied neuropsychiatric manifestations post-EFV initiation, while two children experienced acute neuropsychiatric symptoms that ceased only upon EFV discontinuation, suggesting a potential link to EFV metabolism (Hammond et al., 2019). However, it should be noted that the study faced limitations due to its retrospective nature, lacking baseline cognitive assessments, and an absence of controlled EFV timing, impeding a direct causal link between EFV and neuropsychiatric manifestations.

Globally, as of 2022, approximately 82% of pregnant women living with HIV had access to cARTs to prevent transmission of HIV to their child (UNAIDS, 2023). However, as more children are born to women with HIV who receive ART during pregnancy, concerns have emerged regarding the potential impact of in utero exposure to ARVs. Research suggests that in utero exposure can induce metabolic dysregulation in immune cells of children born to HIV-infected mothers (Mataramvura et al., 2023). Maternal HIV infection itself, combined with the use of ART, may cause mitochondrial dysfunction, altered oxidative phosphorylation, and increased production of reactive oxygen species, impacting immune cell viability and response functioning (Mataramvura et al., 2023). The clinical implications of metabolic dysregulation due to ARV exposure in utero remain poorly understood. Studies indicate higher morbidity and mortality rates among HIV-exposed uninfected (HIV-EU) and HIV-exposed infected (HIV+) children compared to their HIV-unexposed peers (HIV-UU), suggesting potential long-term consequences of altered immune responses (Afran et al., 2014; Dauby et al., 2012; Slogrove et al., 2016). Furthermore, ARTs that interfere with mitochondrial function may lower energy production in the form of adenosine triphosphate (ATP) and increase reactive oxygen species (ROS), potentially affecting neuronal growth and synaptic plasticity (Mataramvura et al., 2023). Moreover, ATP is essential for the activation of immune cells as mitochondria serve as the primary energy source for this process. Additionally, ROS activate proinflammatory signalling pathways, further emphasising the central role of mitochondria in immune response establishment and maintenance (Mataramvura et al., 2023). In HIV infection, both the virus and ARTs can alter mitochondrial functioning, contributing to chronic immune activation and inflammation, ultimately exacerbating HIV immunopathogenesis (Mataramvura et al., 2023).

A longitudinal study assessing the impact of HIV infection and ARVs on the neurocognitive outcomes of 370 mother-child pairs (aged 7 to 14 years), with 55.1% HIV-UU; 7.0% perinatally HIV-EU; and 37.9% perinatally HIV-infected (PHIV) was conducted in Rakai, Uganda (Brahmbhatt et al., 2017). Differences in schooling, gender, and neurocognitive outcomes were evident among these groups. The KABC II was used to evaluate sequential and simultaneous processing, learning, planning, knowledge, and the fluid crystalised index to gauge overall functioning. Adjusted Prevalence Rate Ratios (adjPRR) by age were estimated using multivariable generalised linear models. No significant differences were observed in neurocognitive measures between PHIV and HIV-UU children at baseline. The duration of ART among PHIV children correlated positively with improved sequential processing skills (25–36 months: adjPRR=0.55, CI: 0.34–0.9; 3748 months: adjPRR=0.39, CI: 0.2–0.76; 49+ months: adjPRR=0.23, CI: 0.1–0.54), but did not significantly affect other neurodevelopmental performance on the KABC II (Brahmbhatt et al., 2017). It is important to acknowledge the study's limitations, such as challenges in maintaining full follow-ups for all children on ART and the relatively small size of the HIV-exposed uninfected group, which may have affected statistical power. Nonetheless, these results emphasise the importance of timely ARV initiation.

In another study, the neurodevelopment of HIV-infected infants (n=27) on Highly Active Antiretroviral Therapy (HAART) was compared to HIV-EU (n=29) infants, all under a year old, at the Empilweni Clinic at Rahima Moosa Mother and Child Hospital, South Africa (Whitehead et al., 2014). Using the Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley III), the study assessed the neurodevelopment of HIV+ infants before initiating HAART and then over six months while on the treatment. Results indicated that infant participants with HIV scored significantly lower in motor and language development compared to HIV-EU infants at baseline, three months, and six months follow-up (Whitehead et al., 2014). Although there were no decreases in developmental scores over time, there were also no significant improvements in language ($p=0.46$) or motor function ($p=0.91$). Cognitive development in the HIV group was notably lower initially (*p=0.003*), but by the six-month follow-up, there were no significant differences (*p=0.18*) between the two groups. The study suggests that while HAART might prevent further delays, it did not reverse the neurological damage already present in the cohort of HIV-positive infants (Brahmbhatt et al., 2017).

As such, while ARV use has significantly improved the management of HIV, concerns persist regarding potential neurotoxicity and long-term neurodevelopmental outcomes, especially in children exposed to HIV and ART in utero. These studies underscore the importance of timely initiation of ARVs and ongoing research to better understand and address neurocognitive challenges in individuals living with HIV. The next section will discuss the neurocognitive development of EFs, as well as their importance to daily functioning and relevant methodological issues that arise in their assessment.

Executive Functions and Neurocognitive Development

In light of extensive research discussing the profound impact of HIV on neurocognitive development, it is evident that EFs emerge as a crucial area of concern in the context of paediatric HIV. The interplay between HIV-associated neuroinflammation, neurodegeneration, and disruptions in key neural circuits like the fronto-striatal network, underscores the heightened susceptibility of EFs to impairment in this population. Research on EFs in children has predominantly relied on adapting theories originally developed for adults, however few developmentally based approaches exist. For example, Zelazo and Müller's Hierarchical Model of Executive Functioning (2002) focuses on the complex interplay between EFs within a hierarchical structure. Inhibitory control (the ability to suppress irrelevant or automatic responses), WM (the capacity to temporarily hold and manipulate information), and cognitive flexibility (adaptability to changing tasks or demands) form the foundation for higher-order executive processes, and operate at three levels: control processes, supervisory attentional system, and self-regulation (Zelazo & Müller, 2002). At the control processes level, individuals engage in cognitive tasks that require inhibiting automatic responses, holding information in mind, and switching between tasks or mental sets. The supervisory attentional system oversees these processes, directing attention and allocating cognitive resources based on task demands. Finally, self-regulation involves the ability to monitor and adjust one's own thoughts and behaviours to achieve goals effectively. Together, these levels interact dynamically to support

EFs, allowing individuals to plan, problem-solve, and adapt to changing circumstances in their environments (Zelazo & Müller, 2002). The model delineates how these functions integrate and interact, regulating attention, behaviour, and decision-making, and showcases their evolution from childhood to adulthood, highlighting the developmental trajectory of EFs (Zelazo & Müller, 2002). Despite its valuable framework, some critique this model for potentially oversimplifying the dynamic nature of EFs (Jacques et al., 2009). Nevertheless, it remains a foundational guide in comprehending the intricate cognitive control mechanisms underlying behaviour.

Another example is Masten and Cicchetti's (2010) Developmental Cascade Model, which offers a comprehensive view of development as a dynamic interplay between cognitive systems across time. This model emphasises the cascading effects of early experiences on multiple domains of development, illustrating how events or influences in one domain can trigger a chain reaction impacting various aspects of an individual's growth (Masten & Cicchetti, 2010). The Cascade Model (2010) suggests that early disruptions in EF can have cascading effects on other developmental domains, affecting academic achievement, socioemotional competence, and behavioural regulation in later stages of development. Despite challenges in empirical validation, this model remains instrumental in understanding the intricate and cumulative influences on developmental trajectories (Masten & Cicchetti, 2010). However, it's noteworthy that the scarcity of theories exclusively tailored to EF in children indicates a pressing need for further research to delineate specific developmental mechanisms governing EF in childhood.

A commonly used model of executive functioning is Miyake and Friedman’s Unity and Diversity model (Miyake et al., 2000; Miyake & Friedman, 2012). The model recognises the following three factors: cognitive flexibility (set-shifting), updating (management of WM) and inhibition (of prepotent responses). The use of factor analysis to identify these three specific executive controls is a clear advantage of this model as each of these aspects are already tied to established measures, making them relatively simple to operationalise in a study (Doebel, 2020). While this model proposes that these core EFs are connected and share common skills and controls, they are also defined separately by their distinct functions, establishing a pattern explained as unity and diversity (Friedman & Miyake, 2017). Firstly, inhibitory control is the ability to deliberately prevent an (often automatic) response (Miyake et al., 2000). This refers to both self-control, which is the ability to resist impulsivity, and interference control, which is the ability to direct cognitive control and avoid irrelevant interference (Diamond, 2013). Secondly, updating refers to the active management of WM contents, including their constant monitoring and their reconfiguration when new information comes in and old information is discarded (Miyake & Friedman, 2012). Finally, cognitive flexibility, is the ability to creatively explore alternative perceptions, and appropriately adapt to situational changes (Miyake & Friedman, 2012). Together, these core EFs control major aspects of daily operation, such as the ability to be present, motivated, organised, decisive, publicly aware and socially interactive (Miyake & Friedman, 2012).

Although this model was initially established within an adult population, limited studies have employed this framework to elucidate EF development in younger populations (Brydges et al., 2014; Nyvold et al., 2022). For example, a longitudinal study in Australia explored the developmental trajectory of EFs in 135 children aged between 8–10 years (Brydges et al., 2014). Over a two-year period, the researchers tracked alterations in inhibition, WM, and cognitive flexibility measures in these participants, revealing a significant transition in the structure of EFs as the children approached 10 years of age (Brydges et al., 2014). Initially resembling a singular, undifferentiated construct in younger children, EFs began to manifest as distinct yet interrelated factors as the participants approached the age of 10 (Brydges et al., 2014). These observations align with previous studies establishing a consistent pattern of a unitary model of executive functioning in very young children, transitioning into a 'unity and diversity' model around 10–11 years of age (Brydges et al., 2012; Wiebe et al., 2008; Willoughby et al., 2012; Wu et al., 2011; Xu et al., 2013).

Illustrating this, an investigation into EFs of 243 typically developing preschool children aged 2.3–6 years indicated a unitary model as the most suitable representation of executive control (Wiebe et al., 2008). Additionally, the study found no structural differences in executive functioning between younger (2 years 4 months – 3 years 11 months) and older (4 years 0 months – 6 years 0 months) children, highlighting the consistency of this unified cognitive construct across early childhood (Wiebe et al., 2008). Similarly, a study involving 1,292 five year old children, primarily from low-income backgrounds, explored EFs in early childhood through a newly developed battery of EF tasks (Willoughby et al., 2012). These tasks, validated for use across diverse SES environments, collectively reflected a single-factor structure, also signifying a unified cognitive construct underlying EF performance in this age group (Willoughby et al., 2012). Furthermore, in a study involving 215 typically developing children aged 7–9 years, various measures of inhibition, WM, and cognitive flexibility were examined (Brydges et al., 2014). When applying the Miyake et al. (2000) model, a single-factor structure emerged as the optimal fit, indicating a unitary nature of EFs in children up to 9 years old (Brydges et al., 2014). While behavioural performance showed improvement between these age groups, the underlying structure of EFs remained unified across this age range (Brydges et al., 2014). Thus, pervasive patterns in the literature suggest that during the early to mid-childhood period, up until approximately the age of 9 years, EFs exhibit a unified structure. In other words, a one-factor model of executive functioning appears to be the most suitable representation of the EF in early childhood.

After the age of 9, individual EFs start to differentiate, and by the age of approximately 10 years, the Miyake et al. (2000) Unity and Diversity model of EFs becomes relevant in children (Brydges et al., 2014). For example, a study exploring the developmental facets of EFs in 185 school-aged children (mean age 10.34 years, SD= 3.035) identified distinct developmental variations, affirming a multi-component trajectory in EF maturation (Wu et al., 2011). Through structural equation modelling, three primary components of EF were identified: cognitive flexibility, updating WM, and inhibition; thus concluding that a comprehensive three-factor model best explained the interrelation between these components within this sample (Wu et al., 2011). This age-dependent structure of EF development is further demonstrated in a study which explored cognitive shifts across a sample of 457 participants aged between 7–15 years old (Xu et al., 2013). Participants undertook tasks assessing WM updating, inhibition, and cognitive flexibility, and CFA was used to compare the fit of five models across the various age groups (Xu et al., 2013). The findings indicated a single-factor EF model as the best fit for 7–12 year olds, representing a unified EF with varying degrees of variance (Xu et al., 2013). However, in older children a three-factor model incorporating WM updating, inhibition, and cognitive flexibility emerged as the best fit, suggesting that while measures of these EF components may share underlying cognitive processes in early childhood, distinct developmental dissociations manifest as children transition into adolescence (Xu et al., 2013). In summation, through factor analyses, it was discovered that EFs exhibit an age-related pattern, starting with a unified factor in early childhood and evolving into three distinct factors in late childhood/early adolescence: inhibitory control , set-switching, and updating WM (Menu et al., 2022). As such, the Miyake and Friedman Unity and Diversity model provides a well-supported and suitable framework to explore EFs in children, especially those over the age of 10, as is relevant to my sample.

This age-dependant maturation structure is further elucidated by research on the development of the prefrontal cortex and its correlation with EF in children (Fiske & Holmboe, 2019). It is likely that developmentally based synaptogenesis of the prefrontal cortex contributes to EF abilities in children (Escobar-Ruiz et al., 2023; Hoskyn et al., 2017). Studies utilising functional near-infrared spectroscopy (fNIRS) have consistently demonstrated a strong association between the activation of prefrontal regions and EF tasks in typically developing children (Fiske & Holmboe, 2019; Moriguchi & Hiraki, 2009; Tsujimoto, 2004). Notably, the engagement of prefrontal areas during cognitive flexibility, inhibitory control, and WM tasks mirrors the advancements in EF skills during childhood (Moriguchi & Hiraki, 2011; Tsujii et al., 2009). Developmentally atypical populations, such as children with attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (ASD) exhibit irregular prefrontal activation patterns during EF tasks (Fiske & Holmboe, 2019; Moriguchi & Hiraki, 2009), suggesting a potential link between EF impairments and altered prefrontal development (Moriguchi & Hiraki, 2011). These results underscore the critical role of the prefrontal cortex in EF development in children and highlight how variations in prefrontal activation may manifest in atypical populations as dysregulated EFs (Moriguchi & Hiraki, 2009, 2013; Tsujii et al., 2009).

A clear advantage of operationalising EFs by the Unity and Diversity Model is it separates EFs into three distinct factors, allowing for comprehensive variable analysis (Friedman & Miyake, 2017). While literature exploring the effects of HIV infection on EFs exists, these studies often use single measures of EF, or focus on a single EF (e.g. Milligan & Cockcroft, 2017 who focused on WM). These studies highlight a common trend in EF research where studies rely on single measures, which can be reliable as standardised measures, however have limited construct validity in capturing the multifaceted nature of EFs (Smolker et al., 2018). These limitations in assessing the nature of EF underscore the broader challenges faced in understanding these cognitive processes in both typical and atypical populations. The following section adds to this discussion by addressing the challenges faced in measuring EFs.

Measuring EFs in Children

While accurate assessment of EFs is pivotal in understanding a child's cognitive development, it poses significant challenges due to the multifaceted nature of these functions (Gerst et al., 2017). There are two primary methods in evaluating EF performance in children: cognitive measures and behavioural rating scales. Cognitive measures are standardised tests and tasks designed to evaluate specific cognitive processes such as WM, inhibitory control and cognitive flexibility, and typically involve structured and controlled settings (Gerst et al., 2017). However, this structured nature may in turn affect the ecological validity of these assessments, inadvertently limiting the scope of detecting EF-related issues present in less controlled (everyday) environments (Salthouse et al., 2003). Furthermore, the novelty factor and individualised strategies in EF tasks contribute to divergent approaches, affecting the reliability of cognitive measures (Hughes & Graham, 2002). This variability hampers consistent correlations between EF measures over time or among different assessments (Hughes & Graham, 2002; Miyake et al., 2000).

On the other hand, behavioural rating scales offer a more contextualised assessment by drawing on insights from guardians such as parents and/or teachers. These scales aim to capture observable behaviours related to EFs, including impulse control, organisation, planning, and emotional regulation (Gerst et al., 2017). Unlike cognitive measures, behavioural rating scales provide a contextualised assessment, offering insights into a child's EF patterns in diverse settings, including home and school environments, correlating with real-world functionality (Isquith et al., 2013). However, these scales have their own set of challenges, including rater biases and the limitation of providing only overall scores, failing to dissect specific observed behaviours (Reynolds & Kamphaus, 2004). While more recent rating scales, like the BRIEF, offer subscales targeting specific EF domains, inconsistencies across studies persist, emphasising the need for more refined and detailed assessment approaches that go beyond global scores (Gioia et al., 2000). Behavioural rating scales serve as valuable tools in assessing EFs, yet their limitations and potential biases underline the importance of considering multiple sources of information for a comprehensive understanding of a child's EF profile (Gerst et al., 2017).

Moreover, the relationship between cognitive measures and behavioural rating scales in assessing EFs in children remains uncertain with various studies presenting contrasting findings regarding the correlation between these two assessment methods. Some investigations report weak associations between cognitive measures and behavioural rating scales, indicating a lack of consistent alignment between performance in controlled cognitive tasks and observed behaviours in naturalistic settings (Toplak et al., 2013). For instance, research exploring the association between performance-based measures and rating measures of EFs, intended to ascertain whether these two assessment methods tap into the same underlying cognitive construct (Toplak et al., 2013). The systematic review analysed 20 studies comprising 13 child and seven adult samples derived from clinical, nonclinical, and combined clinical and nonclinical populations. Within these studies, a total of 286 correlations were examined, with only 24% of them (68 correlations) demonstrating statistical significance (Toplak et al., 2013). The median correlation across all studies was a modest $r=.19$, and led the researchers to conclude that performance-based measures and rating measures of executive function potentially assess distinct constructs (Toplak et al., 2013).

Conversely, other studies have highlighted significant correlations between specific EF processes assessed through cognitive measures and corresponding behaviours captured by behavioural rating scales (Shimoni et al., 2012; Toplak et al., 2008). For example, a study focused on EF difficulties in 25 boys aged 8–11 years with ADHD and an equivalent number of age-matched typically developing boys (Shimoni et al., 2012), assessed EF with both the Behaviour Assessment of Dysexecutive Functions for Children (BADS-C) and the BRIEF. These tests were administered independently to each group and the results compared to discern differences in EF (Shimoni et al., 2012). Significant correlations were observed between the BADS-C and BRIEF, particularly in the domain of metacognition (Shimoni et al., 2012). Additionally, research into performance-based measures and ratings of EFs in adolescents with ADHD compared to control groups explored the relationship between cognitive measures and guardian-reported scales (Toplak et al., 2008). Assessments involved performance-based measures targeting inhibition, WM, cognitive flexibility, and planning, while parents and teachers provided ratings on these same EFs (Toplak et al., 2008). The study revealed significant associations between the performance-based measures and the ratings provided by parents and teachers (Toplak et al., 2008). Such variations in correlation strengths underscore the complexity of EF assessment and highlight the necessity of further research into the correlations between cognitive measures and behavioural rating scales. Therefore, the current study incorporated both performance-based measurement of EFs (i.e. the NEPSY-II) and a behaviour rating scale of these abilities (i.e. the BRIEF) in children and adolescents with HIV.

Aside from the challenges facing the measurement of EFs in children, there are various confounding factors that may impact the developmental trajectories of EFs. The academic and socio-behavioural correlates of EFs in children are deeply intertwined with the developmental structure of EFs. The examination of these factors not only elucidates the complexity of EFs but also sheds light on their implications for academic achievement, socioemotional competence, and behavioural regulation in varying developmental stages.

Executive Functioning and Academic Achievement

Growing research has investigated the relationship between EFs and academic achievement. Children with stronger executive skills tend to perform better in academic tasks, including reading comprehension, mathematical problem-solving, and written expression (Best et al., 2011; Bull et al., 2008). These findings reiterate the importance of EFs in supporting academic success and achievement.

For example, a study explored the relations between EF and academic achievement in a large sample (*n = 2,036)* of children, aged 5–17, based in the United States of America (Best et al., 2011). The analysis of a sub-sample (n = 1,395) using the Woodcock–Johnson Tests of Achievement–Revised (1989) indicated that although the relationship between EFs and academic performance changed with age, the developmental pattern of these associations' strengths were comparable for total math and reading achievement (Best et al., 2011). The findings suggested a domain-general relationship between complex EF and academic achievement, highlighting the significance of EFs in shaping educational outcomes (Best et al., 2011). These findings are corroborated by results from similar studies. For example, research conducted in Brazil examined the predictive capacity of EFs concerning reading and arithmetic abilities in elementary school children (Dias et al., 2022). The study involved 94 children aged between 5–7 years (m=6.14, SD=0.65), with 55.3% girls from three public schools in medium-low socioeconomic status environments in Brazil. The study focused on EFs using the Columbia Mental Maturity Scale (CMMS) for nonverbal reasoning, the Simon Task for selective attention, the Cancellation Attention Test for attention ability, the Trail Making Test for preschool children for cognitive flexibility, the Semantic Stroop Test (SST) for inhibitory control, and the Inventory of Difficulties in Executive Functions, Regulation, and Delay Aversion for assessing EF in daily situations through observation by parents/guardians and teachers (Dias et al., 2022). Additionally, academic performance was assessed using the Word and Pseudoword Reading Competence Test and the Arithmetic Test. Notably, children exhibiting stronger EF performance tended to perform better academically, in particular inhibition emerged as a crucial variable in the reading model, and attention and cognitive flexibility were identified as pivotal factors in the arithmetic model (Dias et al., 2022). This trend persisted even after controlling for age and nonverbal reasoning.

Core EFs, such as WM, inhibition, and cognitive flexibility, significantly impact the academic performance of young adolescents, as evidenced by numerous studies emphasising their vital role throughout schooling (e.g. Anabwani et al., 2016; Dias et al., 2022; Follmer, 2018). Specifically, WM (Miller et al., 2013; Pelegrina et al., 2015; Swanson & Jerman, 2007), cognitive flexibility (Guajardo & Cartwright, 2016; Latzman et al., 2010), and inhibition (Borella, Carretti, & Pelegrina, 2010; Fuhs et al., 2015) are identified as significant contributors to reading outcomes. Working memory in particular is often regarded as a predictor of educational achievement (Milligan & Cockcroft, 2017). Various meta-analyses have shown a moderate yet consistent relationship between EFs and academic achievement, particularly in reading and mathematics (Follmer, 2018; Jacob & Parkinson, 2015; Yeniad et al., 2013).

For example, a meta-analytic review explored the relationship between core EFs (WM, cognitive flexibility, inhibition, planning and sustained attention) and reading comprehension, analysing n = 6,673 individuals (Follmer, 2018). There was a moderate positive association between EFs and reading comprehension across the reviewed studies (r = 0.36). Specifically, WM showed a significant correlation (r = 0.38) with reading comprehension, suggesting its importance in maintaining and updating information during tasks that require reading. Cognitive flexibility also demonstrated a significant moderate correlation (r = 0.39), as did inhibition (r = 0.21), although findings were more variable across studies (Follmer, 2018). Planning exhibited a significant moderate correlation (r = 0.36), highlighting its involvement in strategising and organising thoughts during reading tasks. Sustained attention also showed significant correlations with reading comprehension (r = 0.25). Moderator analyses indicated that the correlations between EF and reading comprehension were consistent across various age ranges, types of measures used for both EF and reading comprehension, and the nature of the study.

Overall, the findings underscored the multifaceted nature of EF and its influence on various aspects of reading comprehension, including memory retention, cognitive flexibility, attentional control, and strategic planning (Follmer, 2018).

Another meta-analytical review explored the relationship between children's cognitive flexibility and their performance in math and reading (Yeniad et al., 2013). The study included 18 studies involving n = 2,330 children for math and 16 studies with n = 2,266 children for reading (Yeniad et al., 2013). Various tests were employed to measure set-shifting abilities. These included tasks such as the Trail Making Test, Wisconsin Card Sorting Test (WCST), Flexible Item Selection Task, Contingency Naming Task, Something's the Same Task, Number Letter and Plus Minus Task, Trails Tasks (Trails-P), and Spatial Reversal tasks. These tests assess cognitive flexibility through activities like alternating between numbers and letters, sorting cards based on changing rules, and reversing spatial patterns. Scoring methods varied, with some tasks evaluated based on reaction time, accuracy, efficiency, or a combination of these factors. Cognitive flexibility demonstrated significant correlations with both math ($r = .26$, *95% CI = .15–.35*) and reading ($r = .21$, *95% CI = .11–.31*) performances (Yeniad et al., 2013). These findings emphasised the importance of cognitive flexibility ability in academic tasks, particularly in tasks requiring flexibility in problem-solving strategies, and echo results of other studies suggesting strong links exist between a child’s performance in cognitive flexibility measures and their observed writing skills, arithmetic abilities (St Clair-Thompson & Gathercole, 2006), musical instrument proficiency (González-Andrade et al., 2022), and conscientiousness-related behaviour (Fleming et al., 2016).

In conclusion, the interplay between EFs and academic achievement underscores the critical role EF plays in shaping educational outcomes. Studies reveal a domain-general relationship between complex EF and academic performance, with core EFs such as WM, inhibitory control, and cognitive flexibility significantly impacting academic success. Meta-analytic reviews further solidify these findings, highlighting the multifaceted nature of EF and its influence on reading comprehension and mathematical abilities. While executive skills play a crucial role in academic success, their influence extends beyond the classroom, shaping various aspects of social interaction, emotional regulation, and behavioural adaptability. The following section will discuss the relationship between EFs and socio-behavioural functioning.

Executive Functioning and Socio-Behavioural Functioning

Socio-behavioural functioning encompasses various aspects of behaviour in social contexts, including social skills, emotional regulation, and adaptive behaviours. Executive functioning also plays a vital role in social interactions and adaptive behaviour, and has been linked to social competence in both children and adults (Zelazo et al., 2008). Individuals with well-developed EF skills are better equipped to navigate social situations, display empathy, and resolve conflicts effectively (Best et al., 2011). On one hand, deficits in EFs have been associated with social difficulties, impulsivity, and emotional/behavioural regulation challenges (Best et al., 2011; Willoughby et al., 2012; Zelazo et al., 2008). The prefrontal cortex (PFC), particularly the orbitofrontal cortex (OFC), is a key hub implicated in both cognitive (cold) and behavioural (hot) executive processes (Salehinejad et al., 2021). The lateral PFC, including regions like the dorsolateral prefrontal cortex and ventrolateral prefrontal cortex, along with the dorsal anterior cingulate cortex, are predominantly associated with cold executive functions such as attentional control, inhibition, and WM. On the other hand, the medial and orbital regions of the PFC, such as the ventromedial prefrontal cortex and OFC, along with the ventral anterior cingulate cortex, are closely linked to hot executive functions involving emotional regulation, reward processing, and social cognition (Salehinejad et al., 2021). However, there is considerable overlap and interaction among these regions. For instance, the OFC demonstrates involvement in both cognitive and behavioural domains, integrating information about reward, punishment, and social cues to guide decision-making and adaptive behaviours. Therefore, while distinct functional specialisations exist within the PFC, the complex integration of hot and cold functions underscores the dynamic and interconnected nature of executive processing in the brain (Salehinejad et al., 2021).

Various studies have shown that individuals with impairments in EFs may face challenges when attempting to understand social cues, maintain attention during social interactions, and adapt their behaviour to different social contexts (Hughes & Leekam, 2004; Landa & Goldberg, 2005). A study investigated the relationship between EFs, social interaction skills, and social engagement in adolescents diagnosed with schizophrenia involved 92 participants (62% male; average age = 16.8) who were evaluated four weeks post-hospitalisation, utilising established assessment scales (Madjar et al., 2019). Employing regression mediation analysis and Structural Equation Modelling with bootstrap analysis, the results revealed that EFs significantly correlated with communication skills, which in turn demonstrated a substantial association with social engagement (*indirect effect = 0.29; standardised*; Madjar et al., 2019). Furthermore, researchers had a sample of undergraduate students ($n = 257$) complete an online questionnaire with the intention of determining the importance of EFs for social skills in college students (Hilton et al., 2022). In addition to demonstrating the intricacy of the interaction between EFs and social interaction, the study reiterated findings from previous research by suggesting EFs play a critical function in a variety of social skills and adaptative behaviours (Hilton et al., 2022).

Furthermore, it is important to note the interplay between socio-behavioural functioning, child cognitive and environmental conditions, as highlighted in the pilot study conducted by Fishbein et al. (2019), which explored the impact of a broad range of home environments on EF and behavioural self-regulation in late childhood (ages 8-11 years old). Through the use of the HOME inventory (a structured interview and parent/child observation) and assessment of neighbourhood conditions, the study demonstrates significant associations between home environment and various dimensions of EF and behavioural problems among children from a lower middle-income, working-class sample, emphasising the importance of considering environmental contexts in understanding child development.

As such, research studies such as those discussed above consistently highlight the pivotal role of EFs in fostering communication skills, which subsequently correlate with enhanced social engagement (Hilton et al., 2022; Madjar et al., 2019). These findings emphasise the relevance of EFs in shaping not only individual behaviours but also the quality of social interactions and engagement. In the context of children living with HIV, understanding the intersection of EFs and socio-behavioural functioning assumes a critical role as deficits in EFs can present challenges, impacting the comprehension of social cues, attention maintenance during social engagements, and behavioural adaptability in diverse social contexts (Best et al., 2011; Madjar et al., 2019; Willoughby et al., 2012). As such, recognising and addressing potential challenges to EFs could profoundly influence socio-behavioural functioning within the paediatric population living with HIV. The following section specifically addresses research examining the link between executive functioning and HIV infection in children and adolescents.

Executive Functioning and HIV

In children and adolescents living with HIV, both the severity of infection (indicated by high viral loads and low CD4+ T cell counts) as well as HIV-associated immune activation and inflammation are linked to affected neurocognitive performance (Cohen et al., 2016). As such, dysregulation of cognitive functions linked to HIV may stem from irreversible damage to the CNS occurring prior to the initiation of ARTs (Rowe et al., 2021), ongoing viral replication within the CNS (Chahroudi et al., 2018; Dahl et al., 2014; Sturdevant et al., 2012), continuous or systemic neuroinflammation (Eckard et al., 2017; Kapetanovic et al., 2014; Olivier et al., 2018; Winston & Spudich, 2020) and potential neurotoxic effects of ARVs (Alford & Vera, 2018; Crowell et al., 2014; Hammond et al., 2019). Moreover, HIV may impact EFs in varying ways, potentially influenced by earlier challenges occurring during ‘sensitive periods’ of frontal lobe development, which have been linked to poorer neurocognitive and functional outcomes (Anderson et al., 2010; Jacobs et al., 2007). The vital role of EFs in HIV-contexts is underscored by research identifying the potential impact of EFs on academic achievement (Best et al., 2011; Dias et al., 2022; Follmer, 2018), risk assessment and impulsivity (Walker & Brown, 2018), socio-behavioural functioning (Willoughby et al., 2012; Zelazo et al., 2008) and medication adherence (Alford & Vera, 2018; Nichols et al., 2015). Studies have suggested children living with HIV have a higher risk of neurocognitive impairment and developmental delays when compared to their ‘typically developing’ peers without an CNS disease (e.g. Laughton et al., 2012; Smith et al., 2006). These cognitive impairments arise from structural changes in the brain and manifest across various domains of EF, including attention, WM, language, and motor skills (Debeaudrap et al., 2018; Milligan & Cockcroft, 2017; Rice et al., 2012; Zondo, 2021).

In a cross-sectional study conducted within the Cape Town Adolescent Antiretroviral Cohort in South Africa, the brain structural changes and associated disruption to functioning in n=204 perinatally HIV-infected adolescents (aged 9–11 years) and n=44 uninfected controls were examined (Hoare et al., 2018). The HIV-positive group exhibited significantly poorer performance on the Wechsler Abbreviated Scale of Intelligence (WASI; $p<0.01$), and neuroimaging analyses revealed significant decreases in fractional anisotropy and increases in mean diffusivity among the HIV+ group, alongside reductions in cerebral grey matter volumes, cortical surface area, and gyrification (Hoare et al., 2018). The whole-brain mean fractional anisotropy was notably reduced in the HIV-infected group ($p=0.031$). In adolescents without a CNS disease, stronger WM, attention, and reading-related abilities tend to correlate with higher fractional anisotropy found in the superior longitudinal fasciculus. Correlation analyses showed significant associations, indicating that greater total grey ($p = 0.008$) and white matter volumes ($p=0.004$) were linked to higher scores on the WASI and the Beck Self-Concept Inventory subscale ($p=0.038$). Furthermore, lower whole-brain fractional anisotropy was associated with elevated scores on the Beck Anger Inventory ($p=0.018$) and disruptive behaviour subscales ($p=0.031$), while higher whole-brain mean diffusivity correlated with apathy ($p=0.046$). These findings underscore the pronounced impact of HIV infection on specific neurostructural alterations and their associations with cognitive and mental health parameters during adolescence despite early initiation of ARTs.

Further evidence comes from a cross-sectional observational study conducted at the Wilhelmina Children's Hospital of Utrecht, The Netherlands, school-age children (n =22; median age: 9.46 years) with PHIV infection were assessed for neurocognitive and executive function . Researchers employed a battery of neuropsychological tests and measures alongside the collection of clinical, immunological, and virological data (Koekkoek et al., 2008). Compared to age-matched norms, the HIV+ group showed significantly slower processing speed ($p=0.002$), impaired pattern recognition ($p=0.040$), reduced speed and accuracy in cognitive flexibility tasks ($p=0.001$) and compromised visuospatial memory ($p=0.043$). Verbal fluency was also notably lower than age norms ($p<0.001$). Interestingly, significant correlations emerged between cognitive functions and medical parameters, indicating associations between higher CD4% at HAART initiation and improved accuracy in pattern recognition ($r = 0.62$, $p = 0.01$), as well as longer HAART duration and enhanced speed in cognitive flexibility set tasks ($r = 0.66$, $p = 0.01$). Overall, these findings indicate substantial deficits in EF domains, including cognitive flexibility, visuospatial WM, and verbal fluency, among school-age children living with HIV, despite average intelligence levels, but also suggest potential benefits linked to longer HAART duration and higher CD4% levels at initiation for cognitive outcomes (Koekkoek et al., 2008).

Most research regarding the effects of HIV on executive functioning follows a cross-sectional design (Boivin et al., 2018; Musindo et al., 2018; N. Phillips et al., 2022), with few longitudinal studies providing insights into the long-term effects of HIV infection. One longitudinal study conducted in Amsterdam with n=21 adolescents with PHIV and n=23 HIV− controls (aged 8–18), matched for age, sex, ethnicity, and SES, assessed cognitive development over 4.6 years (Van Den Hof et al., 2019). The neuropsychological assessment covered multiple cognitive domains and was performed by a blinded neuropsychologist using a standardised test battery. Data on demographics, HIV-related characteristics, and cART use were collected and subsequent analyses involved data standardisation, principal component analysis for cognitive domain scores, and statistical modelling to explore associations between HIV status, treatment-related variables, and cognitive outcomes (Van Den Hof et al., 2019). The EFs measured included processing speed, working memory, learning ability, and visual-motor function. Compared to HIV− peers, EFs decreased significantly in the PHIV+ group (group-time −1.43 z score, 95% CI −2.12 to −0.75; p<.001), while trajectories for processing speed, working memory, learning ability, and visual-motor function were statistically unchanged (Van Den Hof et al., 2019). Furthermore, results indicated that starting cART at an older age was associated with greater deviation in EFs (−0.13 z score, 95% CI −0.24 to −0.02; p=.043). Notably, the prevalence of cognitive impairments assessed by multivariate normative comparison remained similar in both groups across both assessment time points (Van Den Hof et al., 2019). This suggests that while ART-treated PHIV-positive adolescents displayed comparable overall cognitive development to their healthy counterparts, deviations in EF trajectories may stem from earlier brain damage caused by HIV infection and may indicate potential cognitive challenges for individuals affected by HIV transitioning to young adulthood (Van Den Hof et al., 2019).

As indicated earlier, findings from several studies support the concept of the three separate, yet interconnected, domains of executive functioning delineated in Miyake and Friedman's (2000) Unity and Diversity Model, namely: updating working memory, cognitive flexibility and inhibition (Lehto et al., 2003; Menu et al., 2022; Miyake et al., 2000; Wu et al., 2011). Although research suggests that individuals infected with HIV can experience a range of challenges associated with EF processes (González-Andrade et al., 2022), evidence specific to children and adolescents is limited (Rowe et al., 2021) and varies greatly in how EFs are operationalised and measured, indicating the need for more research in this area, which is a focus of the current study (Walker & Brown, 2018). The following three sections will discuss the available research on the effect of HIV infection on measures of WM, cognitive flexibility and inhibitory control in children and adolescents.

Pediatric HIV and Working Memory

Working memory, responsible for the continuous modification and manipulation of information, appears particularly susceptible to HIV-related neurocognitive impairments (Milligan & Cockcroft, 2017). Most literature covering WM structural development has relied on the on the theoretical multicomponent model proposed by Baddeley and Hitch (1974); Baddeley (1986, 2000, 2012); and Baddeley et al., (2021). Additionally, this Multicomponent WM Model (Baddeley et al., 2021) is the most widely used in paediatric research (Milligan & Cockcroft, 2017). This model proposes that WM consists of four distinct components: the phonological loop (responsible for the temporary storage of verbal information), the visuospatial sketchpad (handles visual and spatial information), the central executive (directs attention and coordinates the other components), and the episodic buffer (integrates information across different modalities and maintains temporal order). Together, these components enable the temporary storage and manipulation of information required for cognitive tasks, such as problem-solving and decision-making (Baddeley et al., 2021).

There is some support in the literature for differential rates of EF development, with WM maturing first, around adolescence (Diamond, 2012). Among ARV-era HIV-infected individuals, WM appears to be the most significantly impacted of the set of EFs (Walker & Brown, 2018). Specifically, HIV infection of the CNS seems to affect WM processing (mental manipulation and information organisation), but not WM storage (Martin et al., 2001; Martin et al., 2003). This pattern is supported by functional neuroimaging research, which further indicates atypical hyperactivation (characterised by increased blood oxygen level dependent signal) of the WM network, specifically abnormalities in the frontostriatal and frontoparietal circuitry. This hyperactivation suggests a compensatory mechanism within the cortex to overcompensate for neuronal loss, preceding observable changes in behavioural and task performance (Chang et al., 2001, 2017; Tomasi et al., 2006). Studies by Milligan and Cockcroft (2017) and Cockcroft and Milligan (2019) demonstrated deficits in WM tasks among children living with HIV in South Africa compared to their HIV-negative counterparts, which suggest a vulnerability of updating processes to the neuropathological effects of HIV in paediatric populations.

Research examining WM performance among HIV+, HIV-EU, and neurotypical control groups included 273 South African, with balanced gender representation across groups (Milligan & Cockcroft, 2017). Participants (aged 6.19-8.27 years) were grouped as HIV+ (n=95; mean age

= 7.42 years, SD = 0.85), HIV-EU (n=86; mean age = 7.36 years, SD = 0.88), and typically developing controls (n=92; mean age = 7.05 years, SD = 0.86). Working memory was evaluated using composite scores derived from the Automated Working Memory Assessment (AWMA) which measures verbal storage, verbal processing, visuospatial storage, and visuospatial processing (Milligan & Cockcroft, 2017). A multivariate analysis of covariance (MANCOVA) revealed a significant group effect (Wilk's $\lambda = 0.80$, $F(8,526) = 7.98$, $p < 0.0001$), indicating significant differences in performance on verbal and visuospatial composites. Subsequent ANCOVAs revealed the HIV-positive group's significantly poorer performance on WM processing tasks (verbal processing $F(2,270) = 18.16$, $p < 0.0001$; visuospatial processing $F(2,270) = 7.36$, $p < 0.001$), while the HIV-EU group struggled predominantly with verbal WM tasks (verbal processing $F(2,270) = 18.16$, $p < 0.0001$). Within-group comparisons further elucidated these patterns, showing weakness in central executive processing for the HIV+ group and challenges in complex verbal WM processing tasks for the HIV-EU group (Milligan & Cockcroft, 2017). In summary, children living with HIV exhibited WM difficulties, irrespective of modality, reflecting a central executive deficit, potentially linked to frontostriatal white matter network impairment (Milligan & Cockcroft, 2017).

As an extension of the above study, the structural organisation of WM in South African children affected by HIV, in comparison to HIV-EU children and their typically developing peers was investigated (Cockcroft & Milligan, 2019). Employing the AWMA intended to measure WM, the study examined whether WM functioned as a domain-general construct or was fractionated based on verbal/visuospatial domains or maintenance (storage)/manipulation (processing) functions (Cockcroft & Milligan, 2019). Both the HIV-positive and HIV-EU groups exhibited less-defined WM structures, indicating disruption in typical development most likely due to HIV infection and/or exposure. Shared variance across WM constructs in the HIV+ participant group ranged from 48% to 81%, emphasising heavy reliance on executive resources (Cockcroft & Milligan, 2019). In the HIV-EU group, poorer performance on verbal tasks relative to visuospatial ones underlined potential WM difficulties. In summary, results indicated both HIV-positive and HIV-EU paediatric groups exhibited atypical WM organisation compared to their typically developing peers, with children living with HIV facing challenges primarily in WM processing tasks (Cockcroft & Milligan, 2019).

In conclusion, limited research findings consistently highlight the vulnerability of the EF of WM in paediatric HIV populations. HIV infection appears to impact WM processing with implications for both verbal and visuospatial tasks. The following section will focus on the impact of Pediatric HIV on the EF of inhibitory control.

Pediatric HIV and Inhibitory Control

Inhibitory control, or the ability to suppress impulsive responses, plays a pivotal role in adaptive behaviour, attention regulation, risk-taking behaviour management and decision-making (Walker & Brown, 2018). Some studies suggest that HIV infection impacts measures of inhibitory control, with HIV causing functional alterations in brain areas responsible for controlling impulses and behavioural responses (du Plessis et al., 2015). Moreover, during reactive inhibitory control, individuals living with HIV displayed striatal abnormalities such as decreased activation in both the right and left putamen, with significant correlations between markers of glial functioning in the frontal white matter (specifically myo-inositol and creatine) and reduced inhibitory control (Chang et al., 2017; du Plessis et al., 2015). There is a gap in the literature in terms of research relating to the direct measurement of inhibitory control in children and adolescents living with HIV in sub-Saharan Africa. A previously mentioned study (Milligan & Cockcroft, 2017) found significant difficulties in processing tasks across verbal and visuospatial WM modalities. Given the inter-relationship between EFs suggested by the Unity and Diversity model (Miyake & Friedman, 2012), the above WM difficulties suggests that these children may also have potential deficits in inhibitory control-related cognitive processes.

Even on a global scale, very limited research has been conducted on the effects of HIV on inhibition in children and adolescents. For example, conducted within the Pediatric HIV/AIDS Cohort Study Memory and Executive Functioning Study, EFs were investigated in 173 children and adolescents living with PHIV and n=85 PHIV-EU youth (aged 9–18 years) with the Delis-Kaplan Executive Function System (Nichols et al., 2016). The findings highlighted significant differences in inhibitory control among participants living with HIV, who exhibited slower processing speed and increased errors in inhibition tasks compared to the HIV-EU group (Nichols et al., 2016). Notably, the HIV+ group displayed a 13.1% lower mean in Verbal Category Switching ($p = .02$) and a 21.2% decrease in the primary combined score for

Colour-Word Interference (inhibition) compared to PHIV-EU youth (p=.003), underscoring notable disparities in inhibitory control.

Thus, while research indicates that HIV may impact inhibitory control, especially in areas associated with impulse regulation and decision-making, there remains a significant gap in understanding its specific effects on the paediatric population, particularly in sub-Saharan Africa. The following section will focus on the affect HIV infection has on cognitive flexibility abilities in children and adolescents.

Pediatric HIV and Cognitive Flexibility

Among the EF functions critical to everyday functioning, cognitive flexibility, defined as the ability to switch between mental tasks or strategies, also plays a crucial role in adaptive behaviour (Sabat et al., 2020) and decision making (Laureiro-Martínez & Brusoni, 2018). While limited research into the effects of HIV on cognitive flexibility abilities is available, neuroimaging research highlights links between structural and functional brain irregularities in areas like the basal ganglia and medial frontal regions (e.g., dorsal anterior cingulate cortex) and decreased cognitive flexibility abilities in individuals living with HIV (Corrêa et al., 2016; Jiang et al., 2016). As with inhibition, there is very limited research relating directly to cognitive flexibility abilities in children and adolescents living with HIV in sub-Saharan Africa.

In one example, neurocognitive outcomes among HIV+ (n=43), HIV-EU (n=52), and HIV-UU (n=58) groups (aged 3–5 years) were examined in Kenya (Chongwo et al., 2023). Several EFs were measured among children (mean age=4 years old, SD=0.5), including cognitive flexibility, WM, inhibition, receptive language, and cognitive ability. These EFs were assessed using a battery of neurocognitive assessment tests: (i) the A-not-B task, a measure of cognitive flexibility; (ii) the WCST evaluated set-shifting abilities; (iii) the Number Recall Test measured WM; (iv) the Big-small Stroop Test assessed response inhibition and cognitive flexibility (v) the Block Design Task measured cognitive ability; and, (vi) the Picture Vocabulary Test evaluated receptive language skills (Chongwo et al., 2023). Caregiver measures included the Shona Symptoms Questionnaire to screen for common mental disorders and an adapted UNICEF childcare module to assess parenting behaviour. Statistical analyses, including ANOVA and linear regression models, were employed to explore group differences in neurocognitive outcomes and associations with biomedical and psychosocial factors. Notably, results from the cross-sectional study indicate that the HIV-EU group exhibited significantly higher cognitive ability mean scores compared to HIV-UU children ($p = 0.008$). Moreover, improved nutritional status was associated with higher cognitive ability scores ($\beta = 0.68$, 95% CI [0.18–1.18]), while caregivers' symptoms of common mental disorders negatively impacted inhibitory control in children ($\beta = -0.28$, 95% CI [−0.53 to 0.02], $p = 0.036$). Analysis of HIV disease staging displayed larger effect sizes in WM (d= 0.96, CI [0.08–1.80]) and cognitive ability scores (d= 0.83 CI [0.01–1.63]), indicating poorer performance in later stages of infection (Chongwo et al., 2023). The WCST was administered in either Kiswahili or Giriama (Chongwo et al., 2023). While there was no statistically significant difference between the HIV-UU and HIV-EU subgroups ($p = 0.915$), there was a significant distinction between the HIV-EU and HIV+ subgroups ($p = 0.992$) on the WCST, indicating stronger cognitive flexibility abilities in participants who were HIV-EU when compared to those living with HIV (Chongwo et al., 2023).

The limited research on the impact of HIV on cognitive flexibility abilities in children and adolescents, particularly in sub-Saharan Africa, underscores the need for further investigation in this area. Neuroimaging studies have suggested associations between structural and functional brain irregularities in HIV-positive individuals and decreased cognitive flexibility abilities (Corrêa et al., 2016; Jiang et al., 2016). Additionally, a cross-sectional Kenyan study found that children with early-treated HIV (HIV-EU) exhibited significantly higher cognitive flexibility abilities compared to those living with HIV (Chongwo et al., 2023). However, the overall understanding of the effects of HIV on cognitive flexibility in this population remains under-researched.

The multifaceted relationship between HIV infection and the neuro-cognitive functioning of children and adolescents living with the virus reveals a need for further exploration into the specific domains of EF that may be affected. Understanding the nuanced impact of HIV on these distinct domains of executive functioning may provide invaluable insights into the specific cognitive challenges faced by children living with HIV in sub-Saharan Africa, aiding in the development of targeted interventions and tailored support systems. Such research holds the promise of improving the quality of life and cognitive outcomes for these vulnerable populations.

Research Rationale

Antiretroviral therapies have proven effective in reducing the immunological effects of HIV (Vazquez-Santiago et al., 2014). Despite this, high rates of cognitive impairment continue to exist amongst paediatric populations living with HIV (Benki-Nugent & Boivin, 2019). Additionally, a large percentage of the South African paediatric population diagnosed with HIV live in extreme poverty, with a lack of access to adequate psychosocial support and medical care affecting their developmental welfare and academic potential (Cockcroft & Cassimjee, 2020). These socio-economic disadvantages make this population especially vulnerable to the debilitating neurocognitive effects of HIV infection (Dreyer, 2023). Moreover, given the limited understanding of EF in South African children living with HIV, this study aims to contribute a comprehensive evaluation of EF domains using both cognitive measures (i.e. the NEPSY-II) and a behavioural rating scale (i.e. the BRIEF). Given the association between HIV and compromised neurocognitive performance, socio-behavioural outcomes, and academic achievement highlighted in the literature review, this research intends to elucidate the impact of HIV on EF in this population. Understanding EF challenges in children living with HIV can inform tailored interventions to enhance academic, socio-behavioural, and overall developmental outcomes in this vulnerable population.

With this in mind, African-led research is needed to understand the various HIV-associated neurocognitive effects that greatly reduce children's ability to cope with the cognitively demanding tasks of everyday life (Vazquez-Santiago et al., 2014). Furthermore, while literature exploring the effects of HIV infection on EFs in children exists, these research studies often use single measures of EF that limits their construct validity (Smolker et al., 2018). A clear advantage of operationalising EFs in terms of the Unity and Diversity Model (2000) is that it separates these abilities into three distinct factors, allowing for a more comprehensive analysis (Friedman & Miyake, 2017).

Aims and Research Questions

This study conducted exploratory research into understanding EFs in children and adolescents living with HIV in comparison to typically developing peers. The aim was to draw comparisons between the EF performance of the study sample and that of various norm groups (including South African based norms and the manual standardisation samples from both the NEPSY-II and BRIEF). Additionally, this study explored the intercorrelations between the participants' scores on the NEPSY-II subtests and the BRIEF to determine whether these measures tap similar or separate EFs.

Research Questions

This study was directed by two main research questions:

1. *Do HIV+ South African children show compromised executive function compared to the norms from a typically developing paediatric population?*

Null Hypothesis- Ho: HIV+ South African children show no statistically significant difference in executive function test scores compared to those of typically developing HIV- children.

Alternate Hypothesis- Ha: HIV+ South African children show a statistically significant difference in executive function scores compared to those of typically developing HIV- children.

If the results from the first research question prove the Alternate Hypothesis, then the second research question will be addressed:

2. *Specifically, which executive functions are affected in HIV+ South African children living with HIV?*

A secondary research question was:

3. *To what extent do the ratings on the BRIEF correlate with the NEPSY-II scores? (Do the BRIEF and NEPSY-II measures tap similar or different EFs)*

Chapter Two: Methods

Research Design

Epistemologically, this study is situated in a post-positivist paradigm, based on a critical-realist ontology. The post-positivist paradigm moves away from the purely objective stance of positivists, while still emphasising the need for observable, measurable phenomena to form the basis of all knowledge (Fox, 2008). Critical-realism accepts an objective reality, but argues the only way to understand the social world is by understanding the phenomena that generate structures and events (Fox, 2008).

Informed by these paradigms, this research adopted a quantitative, exploratory design approach. This preliminary study followed an exploratory research model as it investigated the under-researched area of potentially dysregulated EFs experienced by children and adolescents living with HIV, with the intention of clarifying these challenges. While literature exploring the effects of HIV infection on EFs exists, these studies often use single measures of EF that may lack construct validity (Smolker et al., 2018). Additionally, few studies focus specifically on EF within the HIV + paediatric population despite South Africa having one of the highest rates of HIV infection globally (UNAIDS, 2022). Consequently, this exploratory study may help to lay the groundwork for more focused research in the future.

The study was non-experimental, with no independent variable researcher manipulation, and data collection was based on pre-existing factors. It utilised observational data collected from the identified population at a single point in time, making it cross-sectional, and as there was no control over the variables of interest (i.e. EFs, HIV infection status etc.), the research design was ex post facto (Fox, 2008). This study used secondary data from a larger pre-test, post-test intervention study titled ‘Customised Cognitive Rehabilitation for a paediatric HIV/AIDS population corroborated by fNIRS: The case of Sustained Attention’ (Zondo, 2021). Subsequently, some aspects of the research design were constrained.

The dependent variables for the study were the three EF components based on the Miyake and Friedman (2000) Unity and Diversity Model: inhibitory control, updating WM and cognitive flexibility. These components were measured using NEPSY-II and BRIEF scores, which are typically treated as continuous variables. The HIV status of the participants was the independent variable. This variable distinguishes between two groups: South African children living with HIV (HIV+ participants) and typically developing children without a CNS disease (based on the norm groups for the BRIEF and NEPSY-II, as well as the NEPSY-II norms established by Truter et al. (2017)). For Truter et al. (2017), norms were derived for South African Afrikaans-, Sepedi-, Sesotho-, Setswana-, Xhosa- and Zulu-speaking children, aged 9–11 and 14–16 years in Grades 4–6 and Grades 8–10 respectively, all from a disadvantaged educational background, making them appropriate for comparison with the study sample. The study was interested in how the participants' EF performance would differ from that of typically developing individuals, as articulated in the research questions.

Participants and Setting

The study was based on a sample of 40 children living with HIV (see results chapter for a detailed summary of the sample's demographic qualities). The secondary data used in this study was collected by Mr Zondo in the contexts of his PhD research, as supervised by Professor Cockcroft. For the overarching study, participants were sourced using a non-probability, convenience sample approach. Participants for the larger study were recruited from three safe-homes for children living with HIV in South Africa. Two of the homes were based in Johannesburg, Gauteng, whereas the third home was located in Makhanda, Eastern Cape. This study focused on the data collected from the Johannesburg-based sample (n= 40). For the overarching study, the inclusion criteria for participants were as follows: (i) children diagnosed as HIV+, who are 7–16 years old; (ii) receiving cART treatment; and (iii) completely unexposed to cognitive rehabilitative therapies (Zondo, 2021). The exclusion criteria were (i) children with illnesses (such as CNS diseases, other than HIV/AIDS) or injury (such as TBI; Zondo, 2021) that may impact neurocognitive functioning.

A priori power analysis was conducted to determine whether the sample (*n=40*) would have sufficient power for the analyses proposed (Faul et al., 2007). This priori power analysis was based on data from Debeaudrap et al. (2018), *n=338*, who compared neurodevelopmental performance in children living with HIV and HIV-uninfected children in Africa. The effect size for the study was d = 0.90, which is considered a large effect, using Cohen's (2003) criteria. With an alpha = 0.05 and power = 0.80, the projected sample size needed with this effect size (G*Power 3.1: Faul et al., 2007) was estimated to be *n = 40* for between group comparisons.

Procedure

With regards to data collection procedures, the administration of the specialised instruments was conducted by an HPCSA registered neuropsychologist. To assess neuropsychological functioning, the NEPSY II neuropsychological test battery (Korkman, Kemp & Kemp, 2007) was used. Sustained attention was assessed using the Conner's Continuous Performance Test (CPT; Conners et al., 2003; Mueller & Piper, 2014). Finally, the school-age version (6-18 years) of the BRIEF was used to evaluate both executive and behavioural functioning (Gioia et al., 2000). All assessment administration was completed in a quiet, secure room at the participant's primary shelter. The timeline and procedure for the overarching study is outlined in Appendix M.

NEPSY-II Comparison Groups

The NEPSY-II sample taken from the NEPSY-II manual norms was based off census data gathered in the United States of America (USA) in 2003 and forms the foundation for establishing standardised norms and reference points for the NEPSY-II assessment across its different subtests and age groups (Korkman et al., 2007). The full sample included 1,200 participants, selected to represent the demographic, cultural, and socioeconomic variations of the population. The age range of the participants spanned from 3–16 years old, capturing crucial developmental stages, and efforts were made to ensure equal representation across genders, ethnicities, geographic regions, and socioeconomic backgrounds (Korkman et al., 2007). By including children from urban, suburban, and rural areas, as well as accounting for differences in educational and cultural experiences, the normative sample aimed to provide a comprehensive understanding of the cognitive and neuropsychological development in children from various contexts within the USA (Korkman et al., 2007). The normative cohort used for comparisons in this study (M = 10, SD = 3, n = 500) were aged between 10–16 years old, and composed of 50% female, 50% male participants.

For comparison to a more appropriately matched South African sample, NEPSY-II data were obtained from a study conducted by Truter et al. (2017). The study included 65 South African children who spoke Afrikaans (n = 49), Pedi (n = 2), Southern Sotho (n = 4), Tswana (n = 3), Xhosa (n = 5), and Zulu (n = 2). The participants were aged 9–11 years (M= 10.64 years; SD = 0.90) and 14–16 years (M= 15.90; SD = 0.68). The younger group was in Grades 4–6, and the older in Grades 8–10. The participants, recruited from various provinces throughout South Africa, primarily from the Western Cape province, came from disadvantaged backgrounds with disadvantaged quality of education. Of the 65 participants, 28 were male and 37 were female. The study aimed to collect preliminary data for the NEPSY-II for disadvantaged children, employing exclusion criteria such as a history of birth complications, neurological disorders, head injury with loss of consciousness longer than one hour, history of psychiatric illness, alcohol or substance abuse, attendance at a special needs school, repeating more than two grades, and a history of learning difficulties.

BRIEF Comparison Groups

The normative sample utilised in the development of the BRIEF comprised a cohort of n=1419 participants, ranging in ages from 5–18 years, with 815 girls (57%) and 604 boys (45%). To ensure the broader applicability of the findings, the samples underwent a weighing process, aligning them with estimated proportions for ethnicity and gender in the United States population. The demographic landscape of the sample included 26.5% of children from urban environments, 59% from suburban locales, and 14.5% from rural settings. The BRIEF manual norms used in this study (M = 50, SD = 10, n = 831) were based on the ages 10–16 years old.

Instruments

Instruments were used to collect information regarding 1) participants' executive functioning (in terms of inhibitory control, updating WM and cognitive flexibility); 2) parent/guardian reports of participants' executive functioning; and 3) participants' demographic characteristics and relevant medical background.

Demographic Questionnaire

It is important to investigate factors that are likely to affect EFs, and therefore the parent or guardian filled out a Demographic Questionnaire to gather important data concerning factors such as gender, age, schooling status, HIV status, and other pertinent information, including TBI status, which was also used to determine eligibility criteria (See Appendix A). Please note, in the case where neither a parent nor guardian was available, the information was supplied by the director of the home of safety.

Neuropsychological Assessment: A Developmental Neuropsychological Assessment (Korkman et al. 2007)

The NEPSY-II is a neuropsychological test that measures cognitive function in paediatric samples (ages 3–16 years of age) (Korkman et al., 2007). It assesses six domains of neurocognitive function: (i) attention and EFs; (ii) social perception; (iii) sensorimotor functions; (iv) visuospatial functions; (v) learning and memory; and (vi) language (Korkman et al., 2007). The EFs the NEPSY-II measures are: attention (selective and sustained), monitoring, planning, inhibitory control, maintenance of response set, self-regulation, cognitive flexibility, vigilance and figural fluency (Korkman et al., 2007). As mentioned, Miyake and Friedman's Unity and Diversity model (2000) defines three components of EFs, namely inhibitory control, cognitive flexibility and updating WM. Various studies have linked the proposed-included NEPSY-II subtest measures with these three components of EFs *(See Table 1 below)*.

Table 1

NEPSY-II Subtests as Indicators for EF Factors in the Unity and Diversity Model (2000)

Author	Inhibition	Updating WM	Cognitive Flexibility
(Faedda et al., 2019)		Word List Interference	
(Rasmussen et al., 2013)		Auditory Attention	
(Beeghly et al., 2014; Dann et al., 2021; Rochat et al., 2017)			Response Set
(Faedda et al., 2019)		Memory for Faces Memory for Faces Delayed	
(Veraksa et al., 2020)	Inhibition-Naming		
(Scott et al., 2017; Veraksa et al., 2020)	Inhibition-Inhibition		
(Klenberg, 2015)	Speeded Naming		
(Dann et al., 2021; Saarikivi et al., 2023)			Inhibition-Switching

Cognitive flexibility was measured using the *Response Set,* and *Inhibition-Switching* subtests, all which aim to evaluate a child's ability to inhibit their dominant response. The

Response Set task assesses a child's ability to switch between two different rules or responses in accordance with changing visual stimuli. In this task, the child needs to adapt to changing instructions and demonstrate cognitive flexibility by switching between rules as the task progresses (Korkman et al., 2007). The scoring for this task involves assessing the child's ability to switch between two different rules or responses based on changing visual stimuli and typically involves measuring the accuracy and speed of the child's response. Response Set is scored based on four measures: RS Total Correct, RS Commission Errors, RS Omission Errors, and RS Inhibitory Errors. RS Total Correct is the primary score for this subtest and reflects the total number of correct responses (Kemp & Korkman, 2010). A low RS Total Correct score suggests poor sustained attention and difficulty in shifting focus. The RS Commission Errors score indicates the number of incorrect responses made when a response should have been inhibited; a high score may suggest either a slow response time, impulsivity, or inattentiveness. While the RS Omission Errors represent the number of correct responses missed, as such, high scores may reflect difficulties in comprehending directions, or challenges to sustained/selective attention. Finally, RS Inhibitory Errors reflect the number of times the individual fails to inhibit a prepotent response, with higher scores potential suggesting impulsivity or difficulty in switching from established behaviours (Kemp & Korkman, 2010; Miller, 2013).

Furthermore, the Inhibition-Switching subtest is designed to assess the ability to switch between different tasks or mental sets. The participant is presented with a set of stimuli and instructed to respond in a specific way to each stimulus; then, the rules are changed, requiring the participant to inhibit the previously learned response and switch to a new response set (Korkman et al., 2007). Two scores comprising this subtest are INS Total Completion Time (primary score) and INS Total Errors. The INS Total Completion Time refers to the total time taken by the child to complete the task, with a slower completion time suggests that the individual’s cognitive processing is affected by the demands of switching between tasks (Kemp & Korkman, 2010). If the completion time is slow and INS Total Errors is low or average, it may suggest that the participant struggles with cognitive processing due to the task demands. Alternatively, a slow completion time coupled with a high number of errors suggests that the child's cognitive processing is slowed by switching demands, and potentially, impulsivity (Miller, 2013).

Updating WM was measured using *Auditory Attention*, *Memory for Faces, Memory for Faces Delayed and Word List Interference*. The Auditory Attention subtest assesses a child's ability to sustain attention and focus on a specific auditory task. Participants are presented with a sequence of auditory stimuli (usually a series of tones) and must respond when they hear a specific target tone. This measures a child's ability to maintain attention and discriminate specific auditory stimuli in a sequence (Korkman et al., 2007). The primary score, AA Total Correct, measures the overall accuracy in responding to auditory stimuli presented (Kemp & Korkman, 2010). The AA Commission Errors score represent instances where the individual responds incorrectly to non-target stimuli, indicating difficulties in inhibiting responses to irrelevant auditory information, whereas AA Omission Errors track the number of times the participant fails to respond to target stimuli, reflecting lapses in sustained attention or auditory processing. Lastly, AA Inhibitory Errors quantify the instances where the individual responds incorrectly to target stimuli, indicating challenges in inhibiting prepotent responses (Miller, 2013).

The Memory for Faces subtest examines a participants' ability to retain and recognise facial features, providing insight into their memory functioning, particularly in the context of facial information processing. A low MF Total Score may imply challenges in the initial encoding or discrimination of new faces (Miller, 2013). On the other hand, Memory for Faces Delayed evaluates the ability to recognise newly learned faces from long-term memory, with a low MFD Total Score indicating difficulties in recognising faces that were previously learned, stored, and retrieved from memory over an extended period (Kemp & Korkman, 2010; Miller, 2013). Furthermore, the subtest Word List Interference evaluates memory and EF in children by assessing their ability to recall words from two different lists after learning them sequentially. The interference occurs as the child must suppress the retrieval of the first list while recalling the second list, and then accurately recall both lists (Kemp & Korkman, 2010). The two primary scores of the Word List Interference subtest are the WI Repetition Total Score and the WI Recall Total. The WI Repetition Total Score reflects the ability to repeat the words from the initial list accurately, with a lower score suggesting a restricted capacity in WM. Conversely, the WI Recall Total measures the ability to recall words from both the initial and interfering lists, demonstrating the capacity to maintain information in WM amid distracting stimuli and multitasking demands. A low score on WI Recall Total implies limited ability to resist interference (Kemp & Korkman, 2010; Miller, 2013).

Finally, inhibitory control was measured using the *Inhibition-Naming, Inhibition-Inhibition and Speeded Namig Subtests.* The Inhibition-Naming subtest is designed to assess a participants' ability to inhibit automatic responses and switch between different cognitive tasks efficiently. The child is presented with a sheet containing rows of symbols and is asked to name each symbol while following specific rules, such as inhibiting the automatic tendency to name a symbol based on its shape or colour (Korkman et al., 2007). The INN Total Completion time (primary score) refers to the total amount of time taken by an individual to complete the naming task in the assessment, thus a low score might indicate poor naming ability, slow processing speed, or a high number of self-corrected errors, whereas INN Total Errors refers to the total number of errors made during the task (Kemp & Korkman, 2010). If the completion time is slow with either a low or average number of errors, it could suggest issues related to psychomotor speed or difficulty with semantic processing. However, if the completion time is slow and there's a high number of naming errors, it may indicate challenges with naming or self-monitoring abilities (Miller, 2013). On the other hand, the Inhibition-Inhibition subtest evaluates an individual's ability to inhibit automatic responses and sustain attention while performing a task, and involves resisting impulses and maintaining focus on the given instructions (Korkman et al., 2007). The INI Total Completion Time refers to the overall time taken by the individual to complete the task, and a low time could suggest slow processing speed. A slow completion time along with a low or average score for INI Total Error implies that inhibitory demands might be slowing down cognitive processing speed. Conversely, a slow completion time along with a high number of errors suggests an impulsive response style and the individual may struggle to inhibit automatic responses effectively (Kemp & Korkman, 2010; Miller, 2013).

For the Speeded Naming subtest, participants are presented with a series of stimuli and are required to name them as quickly as possible, assessing their ability to rapidly name familiar objects, colours, and pictures (Korkman et al., 2007). This subtest is scored based on three measures: SN Completion Time, SN Total Correct and SN Total Self-Corrected. The primary score, SN Total Completion Time, reflects the overall speed of processing and efficiency in verbal labelling, with a low score suggestive of difficulties in processing speed or word retrieval, as well as challenges in producing verbal labels. The SN Total Correct score evaluates the accuracy of responses, with a low score indicating poor self-monitoring or impulsivity in responding. Lastly, SN Total Self-Corrected Errors score measures the ability to recognise and rectify mistakes independently (Kemp & Korkman, 2010; Miller, 2013). High rates of self-corrected errors suggest a balance between impulsive behaviours and compensatory self-monitoring (Miller, 2013).

The standardisation process for NEPSY-II raw scores involves converting them into scaled scores and percentile ranks, allowing for comparison with matched peer groups. Scaled scores are derived by transforming raw scores into age-corrected scores with a mean of 10 and a standard deviation of 3, reflecting a child's performance relative to others of the same age (Kemp & Korkman, 2010). Percentile ranks are obtained by further converting raw scores to age-adjusted scores expressed in a percentile scale, where the scores are grouped into ranges representing different levels of performance. A table describing which scores are scaled and which are interpreted as percentiles can be found in Appendix I. The conversion process involves consulting tables provided in the Clinical and Interpretive Manual, where scaled scores and percentile ranks corresponding to the child's age in years and months are listed (Kemp & Korkman, 2010).

The psychometric properties of two of the NEPSY-II subtests have been validated by the African Health Research Institute through the 'Siyakhula Cohort' study, which included children (aged 7–11 years) from rural South Africa (Rochat et al., 2017). Confirmatory Factor Analysis (CFA) was performed on the three subtests from the NEPSY-II that focused on EF measurement: Auditory Attention, Animal Sorting and Response Set to determine if they loaded on a similar factor. By including these tests along with the Kaufmann Assessment Battery for Children (KABC) subtests related to planning, the study aimed to understand the assessment of EFs within a local sample (Rochat et al., 2017). The results of the CFA indicated that the NEPSY-II subtests formed individual factors, distinct from those in the KABC. This suggests that within the South African context, the NEPSY-II tests used to measure EF retained their distinct properties and did not merge with other cognitive domains assessed by the KABC (Rochat et al., 2017).

Behaviour Rating Inventory of Executive Functioning (Gioia et al., 2000)

The Behaviour Rating Inventory of Executive Functioning (BRIEF) is a neuropsychological assessment for executive and behavioural functioning (Roth et al., 2014). The BRIEF uses a 63-item form and is split into (a) behaviour regulation, and (b) metacognition indexes (Gioia et al., 2000, 2003). The Behaviour Regulation Index (BRI) focuses on a person's ability to regulate their behaviours effectively by assessing impulse control, attention shifts, emotion modulation, and appropriateness of context-driven behaviour (Gioia et al., 2000). Two of the four subtests were included in this study, each of which evaluate a specific facet of behavioural regulation. As a measure of inhibitory control, the first subtest, *Inhibit*, examines a child's ability to control immediate reactions and resist impulsive actions, assessing the capacity to inhibit automatic responses and think before acting (Gioia et al., 2000). The second, *Shift*, serves as a measure of cognitive flexibility, focusing on an individual's capability to transition attention between tasks or activities. Scores for each subtest are then derived from ratings on a Likert scale provided by observers or individuals themselves, with higher scores signifying greater challenges in behaviour regulation (Gioia et al., 2000). Overall, the BRI amalgamates these subtest scores, offering a comprehensive evaluation of an individual's behavioural regulation abilities.

On the other hand, the Metacognition Index (MI), measures a person's ability to think effectively and problem-solve flexibly. It includes items related to the individual's capacity for planning, organisation, WM, and cognitive flexibility (Gioia et al., 2000). Three subtests make up this index, one of which is included in this study as a measure for WM updating. The *working memory* subtest evaluates the individual's capability to temporarily hold and manipulate information for cognitive tasks, highlighting their proficiency in retaining and working with information in their mind (Gioia et al., 2000). As with the BRI, scores for each subtest are obtained through ratings on a Likert scale, either by observers or individuals themselves (Gioia et al., 2000). Elevated scores within this index suggest potential challenges in specific metacognitive functions (Gioia et al., 2000).

Finally, the Global Executive Composite (GEC) provides a comprehensive summary of EF abilities and is derived from the overall scores across all clinical scales of the BRIEF. Elevated GEC scores suggest significant difficulties in EF, encompassing various domains such as inhibitory control, cognitive flexibility, emotional control, initiation, WM, planning, organisation of materials, and monitoring (Gioia et al., 2000). The score standardisation process for the BRIEF involves converting raw scores into T-scores and percentile ranks to facilitate comparison with a normative sample. Raw scores are initially transformed into T-scores (M=50, SD=10) using statistical formulas that adjust for factors such as age and gender. Percentile ranks are then calculated based on these T-scores, indicating the percentage of individuals in the normative sample who scored at or below a given T-score (Gioia et al., 2000).

The BRIEF battery is designed to measure all three aspects of EFs outlined in the Unity and Diversity Model (Roth et al., 2014). Unlike the NEPSY-II, which is a psychometric test administered by a registered professional, the BRIEF is a questionnaire filled out by the participants' caregivers/legal guardians. The benefit of using a caregiver-reported measure is potential for improved ecological validity of the construct of EF (Li et al., 2020). Caregivers can provide longitudinal insights into a child's behaviour across different situations, thus offering a more comprehensive view of the child's executive functioning in their natural environment (Li et al., 2020). Additionally, caregivers have a unique perspective based on various real-life contexts, which can provide valuable information on how a child's EF abilities impact their daily life. However, caregiver responses are subjective, may be influenced by their own perceptions/biases, or may be incomplete or inaccurate accounts of a child's behaviour in different contexts (Bevans et al., 2020). Caregivers may be influenced by social desirability bias, meaning they may underreport or overreport certain behaviours based on what they believe is expected or acceptable (Sanzone et al., 2013). A secondary aim of this study was to investigate the extent to which the caregiver-reported ratings on the BRIEF correlated with the psychometric NEPSY-II scores for both the HIV+ and control groups. This indicated whether the tests are tapping similar or different EFs.

A systematic review evaluated the applicability and validation of the BRIEF, among other psychometric measures aimed at assessing executive and adaptive functioning in low and middle-income countries (LAMICs; Kusi-Mensah et al., 2022). Results indicated that while the BRIEF exhibited strengths in internal consistency and some aspects of construct validity (mainly convergent validity), it lacked sufficient content validity, structural validity, and cross-cultural validity in these settings. Additionally, the quality of evidence varied across different psychometric properties (Kusi-Mensah et al., 2022). Internal consistency demonstrated high-quality evidence in multiple studies across various BRIEF versions. However, content validity, structural validity, and cross-cultural validity showed low-quality evidence or were indeterminate due to methodological issues in the studies reviewed, especially in those employing cross-cultural validation methodologies (Kusi-Mensah et al., 2022). Despite the aforementioned limitations, Kusi-Mensah et al. (2022) concluded that the BRIEF emerged as the most reliable and consistent measure of EF among the paediatric population in LAMICs due to its comprehensive coverage of EF domains.

Ethical Considerations

Before receiving the date or conducting any analyses, ethical approval for this study was obtained from the Humanities Research Ethics Committee (HREC Non-Medical; Protocol Number: MAPSYC /23/07W, see Appendix H). With regards to data collection, the administration of all specialised instruments and assessments were conducted by an HPCSA registered neuropsychologist.

Additionally, the overarching study has received ethical clearance from the University of the Witwatersrand's Human Research Ethics (Medical) Committee, protocol number M211073 (See Appendix B). My study has been added to this project. With regard to the overarching study, permission to recruit participants was sought from the directors of the homes for children living with HIV/AIDS (See Appendix C). Information regarding the study was provided to the parents/legal guardians (See Appendix D). Furthermore, consent was gathered from all parents/legal guardians (See Appendix E), as well as assent from all participants (See Appendix F). This research adheres strictly to the Helsinki Protocol of Ethics guidelines on research with children (World Medical Association, 2001; Zondo, 2021). Therefore, participants and/or their legal guardians were informed their participation was voluntary and could be withdrawn at any point without prejudice. Additionally, both with regard to the overarching research and this study, all steps to ensure anonymity and confidentially were taken. Furthermore, a permission letter from Mr Zondo and their supervisors has been attached as Appendix G. The letter indicates permission to receive the data for the purpose of this specific study. It outlines the scope of the study, the protocol used to protect the participants' identity and the data, as well as the agreements on the extent that the data can be used (e.g., publications). Finally, it was my duty to ensure that no fabrication, exaggeration, or manipulation of data was done in order to reach a predetermined or desired outcome.

Data Analysis

All data was cleaned and organised using the Statistical Package for the Social Sciences software (IBM SPSS- v26). Moreover, the Shapiro-Wilk test was conducted to verify the normality assumptions before any statistical analyses were performed (Shapiro & Wilk, 1965). This test was utilised not only to evaluate the normality of the initial data distribution but also to examine the normality of residuals in the subsequent analyses. Descriptive statistics were then calculated to gain a comprehensive understanding of the data distribution. For all interval variables, means, standard deviations, skewness, kurtosis, and medians (for non-normally distributed data) were calculated.

In order to address the overarching research aim, to establish a profile of EF in a sample of South African children living with HIV, several analytical approaches were employed. Correlation analysis was conducted on the covariates, namely gender and language. This analysis served a multifaceted purpose: firstly, in identifying potential confounding variables within the dataset; secondly, in elucidating cultural and societal influences that could potentially impact EF performance; and lastly, in bolstering the generalisability and validity of the ensuing results. Following this, a thorough examination of the NEPSY-II results was undertaken. This involved a comparison of the results against two distinct sets of norms. Firstly, the NEPSY-II results were compared against the norms established by Truter et al. (2017) specific to the South African population, employing independent t-tests for age brackets spanning 9–11 and 14–16 years. Secondly, the standardised NEPSY-II results were compared against the norms delineated in the NEPSY-II manual (for children aged 10–16), characterised by *M*=10, *SD*=3, and n= 500, utilising independent t-tests for ages 10–16. Similarly, a comparison of the sample's BRIEF T-scores was made with the norms outlined in the BRIEF manual. Specifically, these comparisons were made against U.S.-based norms (for children aged 10–16) with *M*=50, *SD*=10, and n=831, utilising independent t-tests x. In the calculation of t-tests, stringent controls were implemented to mitigate the risks associated with multiple comparisons. Specifically, a Bonferroni correction was applied to regulate possible family-wise error rate, thereby establishing a stricter criterion for the significance of results by recalculating the p-value cutoff (Armstrong, 2014).

For the secondary aim of this study, namely to determine to what extent the parent/teacher ratings on the BRIEF correlate with the NEPSY-II scores, correlational analyses were conducted. Firstly, the extent of correlation between the BRIEF and the NEPSY-II scores was examined. This analysis aimed to unveil the degree of association between these measures, shedding light on potential overlaps or divergences in measuring EFs across cognitive and behavioural domains. Additionally, the interrelationships among various NEPSY-II subtest scores were evaluated to discern the extent of correlation between individual subtests within the NEPSY-II battery. Strong correlations between related subtests were of particular interest, as they could signify consistent measurement of specific cognitive constructs or functions targeted by the assessment tool. Strong correlations between the BRIEF and NEPSY-II scores or among NEPSY-II subtest scores would suggest coherence in measurement, reinforcing the confidence in the assessment instruments to capture and evaluate targeted cognitive domains, inhibitory control, cognitive flexibility and updating WM, reliably and consistently. A more detailed discussion of these analyses can be found in the following chapter.

Data Management

In terms of demographic variables, age was measured as ratio data, while gender, which is considered a dichotomous variable, was coded as dummy variables (1 for male, 0 for female) to integrate it into quantitative analyses while preserving its categorical nature. A summary of each of the dependent variables (inhibitory control, updating WM and cognitive flexibility) is located in Appendix I, as well as an indication of how the scores have been standardised. Scores standardised to percentile ranks, which indicate the relative standing of a score within a distribution, are based on the ordinal scale of measurement. Scaled scores and T-scores are on an interval scale of measurement.

Chapter Three: Results

In Chapter One, the potential for HIV infection in the CNS to cause impairment of EFs in children was discussed and the relevant literature on the topic presented. Chapter Two outlined the research approach, emphasising the adoption of a quantitative, exploratory design to investigate EFs in children living with HIV in South Africa. The primary focus of this study was to establish a profile of executive functioning in children and adolescents living with HIV. The first research question (*Do HIV+ South African children show compromised EF compared to the norms from a typically developing paediatric population?)* and the second research question (*Specifically, which EFs are affected in HIV+ South African children living with HIV?*) were both addressed through independent t-tests and by calculating effect sizes for statistically significantly t-test results. The third research question (*Do the BRIEF and NEPSY-II measures tap similar or different EFs in this sample*?) was examined by correlational analysis between BRIEF and NEPSY-II subtests.

Descriptive Statistics

Normality tests were conducted to check the distributions of the study variables. Furthermore, this section offers an overview of (i) the demographic characteristics and distributions of the participants, including age, gender, grade, language, presence of a TBI and handedness; (ii) NEPSY-II subtest data, both raw scores and standardised scores; and (iii) the BRIEF caregiver-reported data, both raw scores and standardised scores.

Testing Normality

Normality assumptions were investigated using the Shapiro-Wilk test statistic (Mishra et al., 2019) for each dependent variable (Appendix J, Table J1). Furthermore, histograms were produced for each dependent variable (Appendix J, Figures J1 – J27). Considering that normality was violated, non-parametric analyses were favoured where appropriate.

Sample Demographics

The table below (Table 2) provides demographic data of the HIV+ group. The final sample consisted of 40 children (*n=40*), from two children's homes for orphans affected by HIV, based in Johannesburg. Participants were between the ages of 11–16 years old (*M*= 14.65 years, *SD*=1.84 years).

Table 2

Participants' Sociodemographic Profiles

Demographic variable	Frequency	Percent (%)
Gender [n=40]		
Male	17	42.5
Female	23	57.5
School Attendance [n=40]		
Yes	32	80
Special School	5	12.5
No	3	7.5
Grade [n=32]		
Four	2	6.3
Five	1	3.1
Six	2	6.3
Seven	2	6.3
Eight	9	28.1
Nine	6	18.8
Ten	7	21.9
Eleven	3	9.4
Language [n=39]		
isiZulu	15	38.5
isiXhosa	5	12.8
Other	19	48.72
Handedness [n=40]		
Right	38	95
Ambidextrous	2	5
TBI Report [n=40]		
No	40	100

NOTE: All participants were HIV positive. In each case n=40, except 'Grade' where n=32; as three participants do not attend school and five participants do not attend school with registered grades; and 'Language' as one participant did not include their language information.

The majority of participants were female and accounted for 57.5% of the sample. Of the entire sample, 80% attended regular school, while 12.5% attended special schools, and 7.5% did not attend school at all. Notably, grade levels among the school-attending participants varied, with the majority (28.1%) in grade eight, followed by grades nine (18.8%) and ten (21.9%). A smaller proportion was distributed across grades four to seven and eleven.

In terms of language, linguistic diversity was apparent, with isiZulu being the most spoken language (38.5%), followed by isiXhosa (12.8%). Additionally, 48.72% of the sample spoke other languages. Data indicated that 95% of the sample were right-handed, with 5% ambidextrous. None of the participants had a reported history of traumatic brain injury, in line with exclusion criteria prohibiting participants with CNS diseases or neuro-injuries other than HIV/AIDS. The inclusion criteria for the intervention group encompassed age (under 16 years), HIV+ diagnosis, receiving cART treatment, and no prior CCRT exposure.

NEPSY II- Subtest Characteristics

In this study, selected NEPSY-II subtests were administered, which were designed to measure the three distinct aspects of EFs as identified in the Miyake and Friedman (2000) model of unity and diversity: inhibitory control, cognitive flexibility, and updating WM. Inhibitory control was measured using the Inhibition-Naming, Inhibition-Inhibition and Speeded Naming subtests, all of which aim to evaluate a child's ability to inhibit a well-learned response. Updating WM was measured using Word List Interference, Auditory Attention, Memory for Faces and Memory for Faces Delayed. Cognitive flexibility was measured using the Response Set and Inhibition-Switching subtests. Table 3 presents descriptive statistics for the HIV+ group across the various included NEPSY-II subtests. Raw scores were detailed for comparison to the South African norms developed by Truter et al. (2017). Scaled scores were included for comparison to standardised NESPY-II manual norms (Korkman et al., 2007).

Table 3

Descriptive Statistics for HIV+ Group NEPSY-II Subtest Raw Scores and Scaled Scores

		Raw Scores			Scaled Scores		
NEPSY-II Subtest	Variable	Mean	*SD*	Range	Mean	*SD*	Range
Inhibition-Naming	INN Total Errors	4.7	13.48	0-80	-	-	-
	INN Total Completion Time	52.65	32.97	0-231	7.33	3.71	1-19
Inhibition-Inhibition	INI Total Errors	19.1	19.39	0-87	-	-	-
	INI Total Completion Time	77.13	32.48	41-225	5.98	3.53	1-14
Speeded Naming	SN Completion Time	55.08	33.95	27-238	6.90	3.11	1-13
	SN Total Correct	73.9	1.58	68-75	-	-	-
	SN Total Self-Corrected Errors	1.28	1.22	0-4	-	-	-
Word List Interference	WI Repetition	8.13	4.13	2-19	2.20	2.47	1-12
	WI Recall	11.78	5.61	0-25	3.40	3.20	1-12
Auditory Attention	AA Total Correct	23.55	6.37	10-30	3.20*	4.92*	1-12*
	AA Commission Errors	6.1	6.64	0-34	-	-	-
	AA Omission Errors	6.85	6.56	0-20	-	-	-
	AA Inhibitory Errors	20.65	12.95	0-37	-	-	-
Memory for Faces	MF Total Score	10.33	2.49	6-15	7.50	3.21	2-14
Memory for Faces Delayed	MFD Total Score	9.35	2.61	3-15	6.55	2.73	1-13

		Raw Scores			Scaled Scores		
NEPSY-II Subtest	Variable	Mean	*SD*	Range	Mean	*SD*	Range
Response Set	RS Total Correct	25.35	8.77	5-36	2.60*	3.58*	1-9*
	RS Commission Errors	11.3	21.19	0-88	-	-	-
	RS Omission Errors	10.1	8.49	0-31	-	-	-
	RS Inhibitory Errors	9.65	13.13	0-36	-	-	-
Inhibition-Switching	INS Total Errors	42.25	22.19	7-82	-	-	-
	INS Total Completion Time	114.6	38.50	67-271	6.40	3.86	1-15

*NOTE: n=40 in all cases, except * where n=5; - is used when scaled scoring is not available for that subtest*

In Table 3 it is noted that the scaled scores for all subtests are derived from a sample size of n=40, except for the Response Set (RS Total Correct Scaled Score) and Auditory Attention (AA Total Correct Scaled Scores) subtests, where the sample size is n=5. This discrepancy arises from the manual's provision of standardised scaled scoring exclusively for ages 7–12 for these two subtests. Consequently, only five participants from the HIV+ group fell within the specified age range of 7–12, leading to the smaller sample size. For ages 13–16, scores for these subtests are standardised as percentile ranks, as indicated in Appendix I, Table I1. Therefore, the differing sample sizes reflect the age-specific scoring protocols outlined in the manual, ensuring accurate interpretation of the assessment results within the appropriate developmental contexts (Kemp & Korkman, 2010).

BRIEF- Subtest Characteristics

This section presents descriptive statistics on the included BRIEF measures for the sample of South African children living with HIV. In order to assess the performance of the HIV+ sample on the BRIEF in comparison to the standardisation sample, the scores of the HIV samples were transformed into T-scores as outlined in Table 4. In most instances, the HIV sample exhibited remarkably low scores, often falling below the lowest raw-score to T-score conversion range, in which case the lowest available T-score was selected. The was done as an exercise to determine if the BRIEF scores could be usable in comparison with the norm sample's performance, despite a consistently high level of missing responses across the sample. However, as per manual scoring instructions, if the total number of unanswered questions that factor into calculating the scale raw scores is greater than 14, then the BRIEF protocol cannot be appropriately scored (Gioia et al., 2000). This limitation must be considered, as it may render these BRIEF T-scores unusable for interpretation. This is discussed further in the following chapter.

Table 4

Descriptive statistics for HIV+ Group BRIEF Subtest and Index/Composite Raw Scores, as well as Standardised T-scores and Percentile Rank

		Raw Scores		**T Scores**		
Index/ Composite	Subtest	M*(SD)*	Range	M*(SD)*	Range	%tile Rank
BRI		21.11 (5.94)	4-38	44.83(1.77)	36-46	48
	Inhibit	5.14 (1.58)	0-10	45.25(0.68)	44-46	51
	Shift	4.75 (1.44)	2-9	44.86(0.35)	44-45	52
MI		27.06 (5.78)	12-50	42.78(0.97)	42-44	27
	Working Memory	5.31 (1.45)	1-8	43.94(0.91)	43-45	53
GEC		48.25 (10.73)	16-88	42.94(0.91)	42-44	23

NOTE: n=36, BRI= Behavioural Regulation Index, MI= Metacognition Index, GEC= Global Executive Composite

Preliminary Analysis

Conducting correlation analysis for covariates, such as age and gender, serves multiple key objectives. Firstly, it aids in the identification of potential confounding variables, crucial for refining the accuracy of research findings. Secondly, this analysis offers valuable insights into the cultural and societal influences that could impact EF performance, contributing to a more comprehensive understanding of the study's context. Lastly, by exploring correlations with covariates, researchers can improve the generalisability and validity of their results, ensuring that the findings are applicable across diverse populations and settings (Kahlert et al., 2017). Spearman's Rank Correlation is a non-parametric statistical measure that compares the ranked values between two variables, assessing the direction and strength of their monotonic relationship (Field, 2017). Table 5 contains pairwise correlations among the cognitive scores (for measures of inhibitory control, cognitive flexibility and updating WM), and demographic variables (age and gender).

Table 5

Spearman's Rho Correlations Between Age and EF Variables

	Age	AA	RS	INN	INI	INS	MF	MFD	SN	WI REP	WI RC	B-I	B-S	B-WM	BRI	MI	GEC
AA	.466**	-															
RS	.580**	.626**	-														
INN	-.387*	-.377*	-.473**	-													
INI	-.283	-.358*	-.399*	.700**	-												
INS	-.218	-.146	-.147	.253	.540**	-											
MF	.299	.355*	.429**	-.345*	-.217	.031	-										
MFD	0.31	.243	.238	-.349*	-.294	-.168	.239	-									
SN	-.464**	-.380*	-.583**	.519**	.302	.124	-.408**	-.054	-								
WI REP	.484**	.484**	.342*	-.396*	-.230	-.040	.293	.098	-606**	-							
WI RC	.523**	.523**	.400*	-.360*	-.218	-.042	.395*	.130	-.496**	.856**	-						
B-I	-.345	-.098	.007	.122	.072	.322	-.001	-.112	.071	-.267	-.188	-					
B-S	-.063	.086	.098	.074	-.160	.036	.130	-.153	.176	-.190	.046	.369*	-				
B-WM	-.330*	-.207	-.227	.351*	.126	.158	.069	-.168	.318	-.466**	-.461**	.462**	.378*	-			
BRI	-.428**	-.192	-.214	.196	.121	.318	-.006	-.147	.319	-.442**	-.288	.749**	.542**	.462**	-		
MI	-.360*	-.303	-.221	.425**	.126	.217	-.126	-.237	.334*	-.348*	-.350*	.556**	.388*	.670**	.548**	-	

Table 5

Spearman's Rho Correlations Between Age and EF Variables

	Age	AA	RS	INN	INI	INS	MF	MFD	SN	WI REP	WI RC	B-I	B-S	B-WM	BRI	MI	GEC
GEC	-.446**	-.169	-.176	.334*	.095	.319	-.038	-.265	.348*	-.467**	-.348*	.731**	.572**	.654**	.845**	.844**	-

Notes. *n* = 40 for all NEPSY-II subtests: AA= Auditory Attention Total Correct, RS= Response Set Total Correct, INN= Inhibition-Naming Total Completion, INI= Inhibition-Inhibition Total Completion, INS= Inhibition-Switching Total Completion, MF= Memory for Faces Total Score, MFD= Memory for Faces Delayed Total Score, WI REP= Word Interference List Repetition, WI RC= Word Interference List Recall, SN= Speeded Naming Completion Time. *N=36* for all BRIEF subtests: B-I= Brief Inhibit, B-WM= Brief Working Memory, B-S= Brief Shift, BRI= Behaviour Regulation Index, MI= Metacognition Index, GEC= Global Executive Composite

*$p \leq .05$. ; **$p \leq .01$.

Only significant correlations that are related to the strength and direction of the relationship between age and performance on EF measures are described here. The data suggests a consistent relationship between age and various measures of EF. Specifically, there are positive correlations between age and measures of WM, namely Auditory Attention (r(40) = .466, p=.002), WI repetition (r(40)=.484, p=.002), and WI recall (r(40)=.523, p<.001), indicating that these abilities tend to improve with age. Additionally, positive correlations were observed between age and Response Set (r(40)=.580, p<.001), a measure of cognitive flexibility. Conversely, there are negative correlations between age and measures of Inhibition, specifically Inhibition-Naming (r(40)=-.387, p=0.014), Speeded Naming (r(40)=-.464, p=.003) and BRIEF-Inhibit (r(36)=-.345, p=.039). Moreover, age exhibited negative correlations with BRIEF subtests Behavioural Regulation Index (r(36)=-.428, p=.009), Metacognition Index (r(36)=-.360, p=.031), and Global Executive Composite (r(36)=-.446, p=.006).

Furthermore, a point-biserial correlation was conducted to assess the association between the categorical variable of gender and the NEPSY-II and BRIEF EF variables as outlined in Table 6. Gender was dichotomised into male and female categories. None of the correlations between gender and the EF variables yielded statistically significant results.

Table 6

Point-Biserial Correlations Between EF Variables and Gender

	AA	RS	INN	INI	INS	MF	MFD	SN	WI REP	WI RC	B-I	B-S	B-WM	BRI	MI	GEC
Gender	-.090	.018	-.114	-.182	-.071	.131	.001	-.078	-.222	--.299	-.043	.002	.197	.030	.223	.130

Notes. n = 40 for all NEPSY-II subtests: AA= Auditory Attention Total Correct, RS= Response Set Total Correct, INN= Inhibition-Naming Total Completion, INI= Inhibition-Inhibition Total Completion, INS= Inhibition-Switching Total Completion, MF= Memory for Faces Total Score, MFD= Memory for Faces Delayed Total Score, WI REP= Word Interference List Repetition, WI RC= Word Interference List Recall, SN= Speeded Naming Completion Time. *N=36* for all BRIEF subtests: B-I= Brief Inhibit, B-WM= Brief Working Memory, B-S= Brief Shift, BRI= Behaviour Regulation Index, MI= Metacognition Index, GEC= Global Executive Composite

**p* ≤ .05. ; ***p* ≤ .01.

Primary Inferential Statistics

Research Objectives One and Two

The first research question (*Do HIV+ South African children show compromised EF compared to the norms from a typically developing paediatric population?*) and second research question (*Specifically, which EFs are affected in HIV+ South African children living with HIV?*) investigated the differences between EF measures from the HIV+ group and various comparison samples. Independent t-tests were used to determine if there was a statistically significant difference between the means of the HIV+ and these comparison samples. Firstly, the NEPSY-II subtest standardised scores from the HIV+ group were compared to the NEPSY-II manual average scaled score (*M* =10, *SD* = 3; Korkman et al., 2007). The dependent variables of interest were standardised, scaled scores for the primary subtests, namely AA Total Correct, RS Total Correct, INN Total Completion Time, INI Total Completion Time, INS Total Completion Time, MF Total Score, MFD Total Score, WI Repetition, WI Recall and SN Completion Time.

Secondly, the NEPSY-II subtest raw scores from the HIV+ group were compared to those obtained from a HIV- South African cohort of the same age (Shuttleworth-Edwards & Truter, 2023). The dependent variables of interest were subtest raw scores for AA Total Correct, AA Commission Errors, AA Omission Errors, AA Inhibitory Errors, RS Total Correct, RS Commission Errors, RS Omission Errors, RS Inhibitory Errors, INN Total Errors, INN Total Completion Time, INI Total Errors, INI Total Completion Time, INS Total Errors, INS Total Completion Time, MF Total Score, MFD Total Score, WI Repetition, WI Recall, SN Completion Time, SN Total Correct and SN Total Self-Corrected.

Thirdly, the BRIEF scores from the HIV+ participant sample were compared to the BRIEF manual average T-score (*M* = 50; *SD* = 10; Gioia et al., 2000). Here, the dependent variables of interest were t-scores for BRIEF subtests Inhibit, Shift, Working Memory, BRI, MI and GEC. Finally, effect size analysis using Hedges's g was employed on the significant results obtained from the t-tests.

Independent T-Tests

Despite the non-normal distribution of the data, the independent t-test is considered robust due to reliance on the Central Limit Theorem (Field, 2017). Multiple comparisons (family-wise error) were controlled for using a Bonferroni correction, which calculated a stricter p-value cut-off for the significance of results. Firstly, independent t-tests were run to compare the

NEPSY-II subtest performance (raw scores) of the HIV+ group to the South African (raw score) norms from Truter et al. (2017) for ages 9-11 (Table 7) and 14-16 (Table 8). In order to run these analyses, the HIV+ sample was grouped into these two age ranges, delineating the 9–11 age group (n=4, age *M*= 10.50 years, *SD*=0.58) and the 14-16 age group (n=29, age *M* =15.66 years, *SD* =0.67).

Table 7

t-Tests Comparing HIV+ group and South African (SA) cohort (Truter, et al., 2017) on NEPSY-II Raw Scores for ages 9–11

Variable	HIV+		SA		*T*	*df*	*p*	*g*
	M (SD)	*n*	*M (SD)*	*n*				
AA Total Correct	13.50(2.38)	4	27.19(3.49)	16	7.35	18	<.0001*	4.11
AA Commission	12.00(6.78)	4	1.75(3.04)	16	4.68	18	<.0002*	-2.62
AA Omission	17.00(2.94)	4	2.63(3.30)	16	7.93	18	<.0001*	-4.43
AA inhibitory	31.75(7.54)	4	0.69(1.30)	16	16.84	18	<.0001*	-9.42
RS Total Correct	13.25(4.65)	4	31.13(3.10)	16	9.39	18	<.0001*	5.25
RS Commission	42.50(34.12)	4	1.75(1.73)	16	5.20	18	<.0001*	-2.91
RS Omission	21.25(7.32)	4	4.36(3.24)	16	7.19	18	<.0001*	-4.02
RS Inhibitory	32.75(1.71)	4	1.69(1.62)	16	33.98	18	<.0001*	-18.99
INN Total Errors	6.25(4.19)	4	2.00(1.81)	12	2.92	14	.011	
INN Total Completion	54.25(5.06)	4	56.73(10.17)	15	.465	17	.648	
INI Total Errors	23.25(15.17)	4	5.25(3.74)	12	4.12	14	.001*	-2.32
INI Total Completion	79.50(11.09)	4	70.47(15.49)	15	1.08	17	.294	
INS Total Errors	63.50(19.05)	4	9.36(5.82)	11	8.85	13	<.0001*	-5.17
INS Total Completion	92.50(18.19)	4	107.20(21.95)	15	1.224	17	.238	
MF Total Score	9.00(1.63)	4	11.40(1.99)	15	2.21	17	.041	
MFD Total Score	8.75(2.36)	4	11.07(3.06)	15	1.40	17	.180	
WI Repetition	5.50(1.92)	4	15.22(3.21)	18	5.76	20	<.0001*	3.19
WI Recall	7.50(4.20)	4	14.83(6.05)	18	2.28	20	.034	
SN Completion Time	57.50(3.11)	4	61.47(17.30)	17	.449	19	.659	
SN Total Correct	73.00(.816)	4	73.24(1.48)	17	.309	19	.761	

Variable	HIV+		SA		T	df	p	g
	M (SD)	***n***	***M (SD)***	***n***				
SN Total Self-Corrected	1.50(.577)	4	0.65(1.06)	17	1.53	19	.142	

Notes. SD = standard deviation, *df* = degrees of freedom, HIV+ = HIV positive sample, g= Hedges's G (effect size), SA = South African cohort described in Truter et al. (2017). *p≤0.0024

The Bonferroni-adjusted alpha level was approximately $p \leq 0.0024$. Independent t test analysis comparing the HIV+ group NEPSY-II raw scores to published norm data from typically developing South African children aged 9–11 years (Truter et al., 2017), indicated significant differences across various cognitive domains. The HIV+ group scored comparably to the South African (SA) group on most aspects of the subtests tapping inhibitory control. However, the HIV+ group made significantly more total errors on the Inhibition-Inhibition subtest. In terms of subtests tapping WM, the HIV+ group's performance was significantly poorer on the Word List Interference- Repetition and Auditory Attention subtests, with more commission, omission and inhibitory errors made. The HIV+ group performed comparable to the typically developing SA group on measures of Memory for Faces, Memory for Faces Delayed, and Word List Interference- Recall. Finally, regarding cognitive flexibility, the HIV+ group performed significantly worse on the Response Set subtest, with more commission, omission and inhibitory errors made. Additionally, the HIV+ group made significantly more total errors on the Inhibition-Switching subtest but was comparable to the SA group in Inhibition-Switching Total Completion.

Table 8

t-Tests Comparing HIV+ group and South African cohort (Truter, et al., 2017) on NEPSY-II raw scores for ages 14–16

Variable	HIV+		SA		*t*	*df*	*p*	*g*
	M (SD)	*n*	*M (SD)*	*n*				
AA Total Correct	25.34(4.85)	29	28.47(2.18)	17	2.51	44	.016	
AA Commission	5.90(6.91)	29	0.35(0.61)	17	3.29	44	.002*	-1.01
AA Omission	5.03(4.90)	29	1.36(2.09)	17	2.93	44	.005	
AA inhibitory	19.10(12.67)	29	0.41(0.71)	17	6.05	44	<.0001*	-1.85
RS Total Correct	27.66(7.22)	29	33.53(3.18)	17	3.17	44	.003	
RS Commission	9.24(18.65)	29	2.00(4.99)	17	1.56	44	.126	
RS Omission	7.83(6.67)	29	2.00(3.02)	17	3.39	44	.002*	-1.04
RS Inhibitory	6.41(10.77)	29	0.65(0.86)	17	2.19	44	.034	
INN Total Errors	2.24(6.86)	29	1.80(2.14)	20	.28	47	.783	
INN Total Completion	46.76(19.10)	29	48.10(12.13)	20	.28	47	.783	
INI Total Errors	18.10(18.53)	29	3.85(4.39)	20	3.36	47	.002*	-0.98
INI Total Completion	72.41(22.81)	29	60.25(12.24)	20	2.17	47	.035	
INS Total Errors	40.14(22.10)	29	7.55(4.72)	20	6.47	47	<.0001*	-1.88
INS Total Completion	110.86(31.45)	29	96.59(29.91)	20	1.59	47	.118	
MF Total Score	10.62(2.46)	29	12.73(2.69)	22	2.91	49	.005	
MFD Total Score	9.55(2.73)	29	12.86(2.80)	22	4.24	49	<.0001*	1.20
WI Repetition	8.86(4.34)	29	14.00(3.57)	12	3.62	39	.001*	1.24
WI Recall	13.21(5.51)	29	17.92(4.40)	12	2.63	39	.012	
SN Completion Time	49.45(19.26)	29	44.18(12.87)	20	1.07	47	.291	
SN Total Correct	74.24(1.19)	29	74.00(1.69)	20	.584	47	.562	
SN Total Self-Corrected	1.10(1.24)	29	0.70(0.98)	20	1.21	47	.234	

Notes. SD = standard deviation, *df* = degrees of freedom, g= Hedges's G (effect size), HIV+ = HIV positive sample, SA = South African cohort described in Truter et al. (2017). $*p \leq 0.0024$

Independent t-test analyses comparing the NEPSY-II raw scores of the HIV+ group to data for typically developing South African children aged 14–16 years (Truter et al., 2017) indicated significant group differences ($p \leq 0.0024$) across various cognitive domains. The HIV+ group scored comparably to the SA group on most aspects of the subtests tapping inhibitory control. However, the HIV+ group made significantly more total errors on the Inhibition-Inhibition subtest. In terms of subtests tapping WM, the HIV+ group's performance was comparable to the SA group on the subtests tapping Auditory Attention (however, the HIV+ group made more commission and inhibitory errors in the latter), Word List Interference- Recall and Memory for Faces. The HIV+ group performed significantly worse on Memory for Faces Delayed, and Word List Interference- Repetition. Finally, regarding cognitive flexibility, the HIV+ group performed comparably to the SA group on Response Set (however, the HIV+ group made significantly more omission errors), and while the HIV+ group made significantly more total errors on the Inhibition-Switching subtest, they were comparable to the SA group in Inhibition-Switching Total Completion.

Table 9 presents the results of t-tests comparing the primary scaled scores of the HIV+ group to the scaled score norms from the NEPSY-II manual (Kemp & Korkman, 2010). The sample's NEPSY-II raw scores were transformed into scaled scores using the NEPSY-II manual, and these scores were then compared to the manual's norms established for the age group (*M*=10, *SD*=3, n=500). This comparison allows for an examination of how the HIV+ group's performance on included subtests aligns with expected norms for their age group.

Table 9

*t-Tests comparing HIV+ group to scaled, primary scores** from NEPSY-II*

Variable	HIV+		*T*	*Df*	*p*	*g*
	M (SD)	*N*				
AA Total Correct	3.20(4.92)	40	13.02	538	<.0001*	2.14
RS Total Correct	2.60(3.58)	40	14.79	538	<.0001*	2.43
INN Total Completion	7.33(3.71)	40	5.32	538	<.0001*	0.87
INI Total Completion	5.98(3.53)	40	8.04	538	<.0001*	1.32
INS Total Completion	6.40(3.86)	40	7.14	538	<.0001*	1.17
MF Total Score	7.50(3.21)	40	5.05	538	<.0001*	0.83
MFD Total Score	6.55(2.73)	40	7.04	538	<.0001*	1.16
WI Repetition	2.20(2.47)	40	16.01	538	<.0001*	2.63
WI Recall	3.40(3.20)	40	13.32	538	<.0001*	2.19
SN Completion Time	6.90(3.11)	40	6.28	538	<.0001*	1.03

Notes. SD = standard deviation, *df* = degrees of freedom, g= Hedges's G (effect size), HIV+ = HIV positive sample. *p≤0.005 **(M=10, SD=3, n=500)

The Bonferroni-adjusted alpha level was p≤0.005. The t-test results (Table 9) revealed that the HIV+ group scored significantly worse on all subtests tapping measures of inhibitory control, WM and cognitive flexibility compared to the standardisation sample for the NEPSY-II.

Finally, Table 10 presents the results of t-tests comparing the BRIEF subtest results, represented as standardised T-scores, of the HIV+ group to the BRIEF manual norms (*M*=50, *SD*=10, n=831; Gioia et al., 2000).

Table 10

*t-Tests comparing HIV+ group to BRIEF T-Scores scores***

Variable	**HIV+**		***T***	***Df***	***p***	***g***
	M (SD)	*N*				
Inhibit	45.25(0.68)	36	2.85	865	.0045*	0.485
Shift	44.86(0.35)	36	3.08	865	.0021*	0.525
Working Memory	43.94(0.91)	36	3.63	865	.0003*	0.619
BRI	44.83(1.77)	36	3.10	865	.0020*	0.527
MI	42.78(0.97)	36	4.33	865	<.0001*	0.737
GEC	42.94(0.91)	36	4.23	865	<.0001*	0.721

Notes. SD = standard deviation, *df* = degrees of freedom, g= Hedges's G (effect size), HIV+ = HIV positive sample, BRI= Behavioural Regulation Index, MI= Metacognition Index, GEC= Global Executive Composite. *p≤0.0083 **(m=50, SD=10, n=831)

The Bonferroni-adjusted alpha level was approximately p=0.0083. The t-test results (Table 10) revealed that the HIV+ group scored significantly better on all BRIEF subtests, as lower scores signify stronger EFs, compared to the standardised norms from the BRIEF manual.

Research Objective Three

The third research question investigated if the BRIEF and NEPSY-II measures tap similar or different EFs. Spearman's rank correlation analysis (Table 5) was run on the data to examine the extent to which (i) the BRIEF subtests scores significantly correlate with NEPSY-II subtest scores, (ii) the NEPSY-II subtest scores significantly correlate with each other, and (iii) the BRIEF subtest scores with each other. Importantly, higher BRIEF scores signify greater challenges in assessed cognitive domains, as such a negative correlation with NEPSY-II scores tapping similar areas would be anticipated.

Based on the correlations displayed in Table 5, several BRIEF subtest scores appear to be significantly related to NEPSY-II subtest scores. Specifically, BRIEF measures of WM (BRIEF WM) was negatively correlated with NEPSY-II measures of WM: WI Repetition (r(36)=-0.466, p=0.004) and WI Recall (r(36)=-0.461, p=0.005). The WI Repetition subtest score further negatively correlated with the BRIEF’S BRI composite (r(36)=-0.442, p=0.007). The BRIEF’S MI score was positively correlated with NEPSY-II measures of inhibitory control, specifically INN Total Completion Time (r(36)=0.425, p=0.010) and SN Completion Time (r(36)=0.334, p=0.046). Moreover, the MI was negatively correlated with NEPSY-II measures of WM, WI Repetition (r(36)=-0.348, p=0.037) and WI Recall (r(36)=-0.350, p=0.036). Finally, the overall BRIEF GEC was positively correlated with NEPSY-II measures of inhibitory control, INN Total Completion (r(36)=0.334, p=0.046) and SN Completion Time (r(36)=0.348, p=0.037), and negatively correlated with NEPSY-II measures of WM, WI Repetition (r(36)=-0.467, p=0.004) and WI Recall (r(36)=-0.348, p=0.038). Overall, there seems to be consistent correlations between BRIEF subtest scores and NEPSY-II subtest scores, particularly in relation to WM and inhibitory control tasks.

Furthermore, based on the correlations among NEPSY-II subtests (raw score; Table 5), several relationships can be observed. Firstly, measures of WM were inter-correlated, specifically AA Total Correct was positively correlated with MF Total Score (r(40)= 0.355, p=0.25), WI Repetition (r(40)=0.337, p=0.033) and WI Recall (r = 0.509, p < 0.001). Secondly, measures of cognitive flexibility were correlated with the RS Total Correct negatively correlated with INS Total Completion Time (r(40)=-0.146, p = 0.368). Lastly, measures of inhibitory control were correlated with each other; INN Total Completion Time was positively correlated with SN Completion Time (r(40)=0.519, p<0.001), and negatively correlated with INI Total

Completion Time (r(40)=-0.700, p<0.001). Overall, several significant correlations are observed among NEPSY-II subtests that tap related skills.

Finally, based on the correlations among BRIEF subtests (raw score; Table 5), several relationships can be observed. The Inhibit was positively correlated with Shift (r(36)=0.369, p=0.027), WM (r(36)=0.462, p=0.005), BRI (r(36)=0.749, p<0.001), MI (r(36)=0.556, p<0.001), and GEC (r(36)=0.731, p<0.001). Whereas, Shift was positively correlated with WM (r(36)=0.378, p=0.023), BRI (r(36)=0.542, p<0.001), MI (r(36)=0.388, p=0.019) and GEC (r(36)=0.572, p<0.001). WM had positive correlation with BRI (r(36)=0.462, p=0.005), MI (r(36)=0.670, p<0.001) and GEC (r(36)=0.654, p<0.001). BRI correlated positively with MI (r(36)=0.548, p<0.001) and GEC (r(36)= 0.845, p<0.001). Finally, MI was positively correlated with GEC (r(36)=0.844, p<0.001). Overall, the data suggest that the various subtests of the BRIEF are related to each other. Some correlations are particularly strong, such as the correlation between BRI and GEC (r=0.845) and between MI and GEC (r=0.844), indicating a very strong relationship between these constructs.

In conclusion, this chapter provided a comprehensive analysis of the EF profiles of children and adolescents living with HIV in South Africa. Through independent t-tests, significant differences in EF performance were found between the HIV+ group and various comparison samples. Additionally, correlational analysis between the BRIEF and NEPSY-II subtests shed light on the relationship between different EF measures employed in this study. The next chapter interprets these findings in the context of existing literature, addressing research limitations, providing implications for clinical practice, and proposing avenues for future research to better support young people living with HIV in South Africa.

Chapter Four: Discussion

Context for the Research Problem

The prevalence of paediatric HIV, particularly in regions like sub-Saharan Africa, remains a significant global concern (UNAIDS, 2023). Despite advancements in reducing vertical transmission rates and increasing access to ARVs, children living with HIV still face considerable challenges, including neurocognitive impairments associated with the infection (Benki-Nugent & Boivin, 2019). These challenges, influenced by factors such as disease progression, immune activation, inflammation, and potential ARV neurotoxicity, vary in severity (Phillips et al., 2018). Specifically, HIV impacts the integrity of the fronto-striatal circuit and CEN, disrupting fundamental neural systems responsible for EFs (Britz & van Zyl, 2020). Executive functions are cognitive processes essential for guiding goal-directed behaviours, and disruption of these neural networks profoundly affects not only academic performance but also social functioning and overall quality of life for children and adolescents living with HIV (Anabwani et al., 2016). By examining the three specific domains of EFs, namely WM, inhibitory control, and cognitive flexibility (Miyake et al., 2000), this study aimed to provide insights into the EF challenges faced by HIV-positive South African children and adolescents in relation to their typically developing peers, ultimately contributing towards understanding the neurocognitive impact of HIV in paediatric populations.

However, due to their multifaceted nature, measuring EFs in children poses several challenges. Cognitive measures and behavioural rating scales offer methods to evaluate EF performance, each with advantages and limitations (Gerst et al., 2017). Studies exploring the correlation between these assessment methods present mixed findings. One study reported weak associations, suggesting they may tap into different underlying constructs (Toplak et al., 2013), while other studies have found significant correlations between the measures (Shimoni et al., 2012; Toplak et al., 2008). As such, this study aimed to examine correlations between NEPSY-II subtests and the BRIEF to better understand the relationship between these cognitive measures and behavioural rating scales in assessing EFs in children with HIV. Additionally, considering the challenges and limitations associated with each method, a comprehensive approach that incorporated multiple sources of information was essential for obtaining a more comprehensive profile of EF in children and adolescents with HIV.

Reiteration of the Research Questions

This study was directed by three research questions:

4. *Do HIV+ South African children show compromised executive function compared to the norms from a typically developing paediatric population?*
5. *Specifically, which executive functions are affected in HIV+ South African children living with HIV?*
6. *To what extent do the ratings on the BRIEF correlate with the NEPSY-II scores? (Do the BRIEF and NEPSY-II measures tap similar or different EFs in this sample)*

Exclusion of the BRIEF Results from Interpretation

Upon examination of the collected data, it became evident that the exceptionally low scores observed on the BRIEF were not suggestive of above-average cognitive function. Rather, they indicated a significant number of missing responses within the BRIEF questionnaire for each of the participants. This is attributed to the fact that, contrary to standard procedure where parents/primary caregivers are tasked with completing the BRIEF, in this sample the questionnaires were filled out by the director(s) of the participant's house of safety. In the case of four children, the director was not available at the time of data collection, so the questionnaires were completed by the onsite nursing staff. Unfortunately, due to their role and perhaps limited familiarity with each child's behaviour, the directors (or nursing staff) were unable to provide comprehensive responses for every individual. The manual cautions against drawing conclusions from BRIEF scores characterised by numerous missing responses, emphasising the potential distortion of outcomes (Gioia et al., 2000).

The Results chapter of this study included an exercise converting BRIEF raw scores to T scores for comparison with the normative sample, but this yielded incorrectly inflated scores which were not interpretable. The inflated scores distort the true representation of the participant's EF abilities, thereby compromising the validity and reliability of any subsequent interpretations or conclusions drawn from the data. This was particularly evident given the compromised EF functioning demonstrated by the NEPSY-II subtest outcomes for the same group of participants. As such, the remainder of the discussion establishing an EF profile for children and adolescents living with HIV will focus solely on the NEPSY-II scores. However, the raw BRIEF scores still serve a purpose as they were utilised to address the third research question, where the aim was not to interpret individual profiles of EF but rather to explore correlations between cognitive and behavioural measures, bearing in mind the above limitations. In this context, the raw BRIEF scores retain their utility as they contribute to the understanding of broader relationships between different aspects of cognitive and behavioural EF measures.

As such, interpretation of the BRIEF is constrained by the prevalence of missing responses and the associated warnings provided in the manual. Researchers should be mindful of the ethical implications of using these scores given the major issue with the nature of the reporting on that scale. Moving forward, it is imperative to acknowledge these limitations and explore alternative measures or supplementary methods, such as culturally sensitive adaptations, to enhance the validity and reliability of the BRIEF cognitive assessment within atypically developing populations.

Demographic Variables and Executive Functioning

Correlational analyses investigated the potential influence that age and biological gender had on EF performance for each measure. While gender and age were not be directly utilised in subsequent statistical analyses, they serve as fundamental demographic variables that offer valuable insights into the composition and diversity of the study population. Moreover, acknowledging these variables allows for the identification of potential sources of variation or bias that could influence study outcomes.

Age and EF Performance

The relationship between age and NEPSY-II measures can be summarised as follows: Positive correlations were found between age and WM measures such as Auditory Attention, WI Repetition, and WI Recall, indicating that, as expected, these abilities improve with age in the sample. Furthermore, there was a positive correlation between age and Response Set, suggesting that some aspects of cognitive flexibility may also improve with age. Negative correlations were observed between age and timed measures of inhibition, Inhibition-Naming total completion time and Speeded Naming total completion time, indicating that as participants age their naming speed improves. Thus, inhibitory control seems to improve with age. This is most likely associated with structural and functional changes in the PFC, and follows expected developmental trajectories for typically developing populations (Hoskyn et al., 2017; Moriguchi & Hiraki, 2009, 2011).

In terms of the BRIEF raw scores, the results indicate that age is negatively correlated with various measures of EF. Specifically, older individuals tend to exhibit lower scores on the BRIEF-Inhibit subtest, as well as on the BRI, MI, and GEC. In the context of the BRIEF, lower scores indicate better performance, reflecting fewer cognitive challenges. Therefore, older participants tend to exhibit lower scores on the BRIEF subtests, suggesting better executive functioning. Given the evidence suggesting that EFs experience a sensitive period of heightened development during childhood and adolescences (Brydges et al., 2014; Escobar-Ruiz et al., 2023; Hoskyn et al., 2017), these findings follow the expected developmental trajectory for typically developing children and adolescents.

Biological Gender and EF Performance

In addition to age, biological gender was measured as a demographic variable in order to determine its possible impact on EF performance. Results indicated that gender did not correlate significantly with any of the EF variables across both NEPSY-II and BRIEF measures. As such EF performance did not differ significantly between males and females in the studied population.

Profile of Executive Function in a Paediatric Sample living with HIV

This section establishes a profile of EFs exhibited by a cohort of South African (SA) children and adolescents living with HIV, addressing research questions one and two. The HIV+ group's NEPSY-II subtest performance is primarily compared to SA norms developed by Truter et al. (2017), for ages 9–11 and 14–16, with the HIV+ sample divided into these age ranges. This comparison group is felt to be more appropriate than the foreign US-based norms (from the NEPSY-II manual), given that the former provides a socio-economically and culturally relevant benchmark for understanding cognitive function within the specific context of South Africa. Using local norms ensures a more accurate assessment of how HIV infection may affect EFs in this population, allowing for better-informed interventions and support strategies. By summarising the relevant findings, the strengths and weaknesses in EF performance among SA youth living with HIV is elucidated, in turn shedding light on critical dimensions of cognitive functioning in this context. The interpretation of these findings was then discussed in relation to existing literature, providing insights into the unique challenges facing cognitive function in paediatric populations living with HIV in South Africa.

Working Memory Updating

With regards to the NEPSY-II subtests measuring WM, several discrepancies were observed when comparing the mean scaled score to the NEPSY-II US-based manual norms (Kemp & Korkman, 2010). For the Auditory Attention subtest, the HIV+ subgroup (participants aged 10–12) performed significantly poorer, and with greater within group variability. The HIV+ subgroup's performance on this task is notably lower than the expected average performance indicated by the NEPSY-II norms. Furthermore, the higher standard deviation for the HIV+ group indicates a greater variability in performance. In terms of the Word List Interference subtest, both primary scaled scores for the Word List Repetition and Word List Recall tasks were extremely low, reporting very large effect sizes indicative of poor performance relative to the expected average. Notably, the HIV+ group performed significantly poorer than the norm group on Memory for Faces (both immediate and delayed subtests), despite the average scaled score on the former falling within the average range (7–13).

Performance on the same WM subtests from the NEPSY-II for the HIV+ group was also compared to SA norms by Truter et al. (2017) for ages 9–11 and 14–16, with the HIV+ sample divided into these age ranges. The HIV+, 9–11 age-group, scored significantly lower than the SA norms on both Auditory Attention and Word List Interference- Repetition, both reporting exceptionally high effect sizes indicating substantial difference between the means of the two groups, mirroring the poorer performance of the overall sample on these subtests when compared to the US norms. Furthermore, the younger HIV+ group performed comparably to the typically developing SA group on measures of Memory for Faces (immediate and delayed) and Word List Interference- Recall. Similarly, the older HIV+ cohort, aged 14–16, performed comparably to the SA norms on the primary Auditory Attention score, although notably made significantly more AA Commission and AA Inhibitory Errors during the task, both reporting large effect sizes. This suggests that their levels of accuracy were similar to the SA norm group, but their process in completing the task was significantly more error based. Additionally, the older HIV+ group performed comparably to the SA norm group on the Memory for Faces (immediate) and Word List Interference- Recall subtests, indicating average performance on these measures. This also suggests that there may be some improvement in the HIV+ group's WM functioning with age, and as their English language skills advance. However, on both the Memory for Faces Delayed and Word List Interference- Repetition subtests, the older HIV+ group performed significantly worse than the SA group with large effect sizes, suggesting that longer-term memory for faces remains an area of difficulty.

These results highlight significant discrepancies in WM performance among HIV+ individuals compared to normative data from both the US (Kemp & Korkman, 2010) and South Africa (Truter et al., 2017). When compared to NEPSY-II norms, participants living with HIV in South Africa exhibited notably lower scores and greater variability on Auditory Attention tasks and, similarly, performed poorly on Word List Interference tasks, with large effect sizes indicating substantial differences. Comparison with SA norms further emphasised these disparities, particularly in younger age groups, while older individuals living with HIV showed some comparable performance on WM measures. These findings align with the broader literature which suggests that WM follows age-specific developmental patterns (Gathercole et al., 2004), and that HIV infection and exposure can disrupt the typical trajectory of WM development (Cockcroft & Milligan, 2019). Specifically, in the younger group, the verbal and visuospatial storage systems appeared distinct, supporting existing claims of separation between these systems and corresponding brain structures (Baddeley, 2000; Baddeley et al., 2021). As such, these findings suggest that among the younger group of children living with HIV, there is evidence of poorer verbal WM and processing in the phonological loop, indicating a reliance on the phonological loop for storage in complex verbal WM tasks. These discrepancies may imply challenges in maintaining and manipulating verbal information within WM, potentially impacting tasks reliant on the phonological loop, such as remembering and processing spoken language or verbal instructions (Cockcroft & Milligan, 2019). Conversely, given that Memory for Faces relies more on visual processing and the visuospatial component of WM, the findings did not reflect the same level of disruption as seen in the verbal tasks. In the context of the younger group, this could suggest that while there may be challenges in verbal WM and processing, the performance on tasks involving visuospatial processing might be relatively less affected. This highlights the importance of considering different cognitive domains and their specific neural underpinnings when examining the impact of HIV on WM and related processes in younger individuals.

Cognitive Flexibility

There were substantial differences noted between the HIV+ group's mean scaled score and the NEPSY-II manual norms on subtests assessing cognitive flexibility (Kemp & Korkman, 2010). The groups differed greatly on the Response Set subtest with a very high effect size, suggesting that the HIV+ subgroup (participants aged 10–12) performed considerably lower than the expected average performance indicated by the NEPSY-II manual norms, with more variability in performance. Although the HIV+ group mean scaled score on the Inhibition-Switching subtest fell just below the average range (7–13), performance was significantly poorer than that of the US norm group, represented by a fairly large effect size.

The cognitive flexibility of the HIV+ group, as assessed using NEPSY-II subtests, was then compared to SA norms established by Truter et al. (2017). The younger HIV+ group, aged 9–11, scored significantly worse on the Response Set subtest, reporting an exceptionally high effect size. Furthermore, while there was no statistically significant difference between the groups on the primary score of the Inhibition-Switching subtest, the HIV+ group did make significantly more total errors on this subtest. The 14–16-year-old HIV+ cohort performed comparably to the SA norms on the Response Set subtests, although made significantly more Omission Errors. Similarly, there were no significant differences between both group's mean scores on the primary measure of the Inhibition-Switching subtest, although the HIV+ group made more total errors on the task.

These findings suggest significant differences in cognitive flexibility between HIV+ participants and normative samples, as well as variations within HIV+ subgroups by age. Compared to NEPSY-II manual norms, HIV+ individuals performed notably lower on all the subtests tapping cognitive flexibility. In comparison to the more appropriate SA norms, the younger HIV group still struggled with measures of cognitive flexibility, specifically switching between different sets of information (as indicated by scores for the Response Set subtest) but managed to perform at an equivalent level on the Inhibition-Switching task. The older HIV group's performance was comparable to SA norms in terms of accuracy. However, both younger and older groups made significantly more errors on most of these tasks than their typically developing peers, suggesting a poor strategy/approach to completing these tasks (and may possibly indicate a higher number of guesses).

Inhibitory Control

There were considerably fewer discrepancies between the sample's mean scaled scores and the US manual norms on the NEPSY-II subtests tapping inhibitory control. Specifically, on the Inhibition-Naming subtest, the HIV+ group obtained mean scaled scores within the average range (7–13). However further analysis revealed statistically significant differences between the group means with a medium to large effect size, indicating below average performance for the HIV+ group. Scores on the Speeded naming subtests felt just below the average range and statistically significant differences were represented by a large effect size. Finally, scores for the Inhibition-Inhibition Subtest were significantly below average with a large effect size, indicating poorer performance on this measure.

Furthermore, the HIV+ group's performance on the same inhibitory control subtests was compared to SA norms established by Truter et al. (2017). Both HIV+ subgroup age groups (9–11 and 14–16 years) performed comparably to the SA norms on the primary measures of all three subtests measuring inhibitory control. However, with regard to the Inhibition-Inhibition subtest, both HIV+ group made significantly more errors during the task.

With regard to this aspect of EF, results indicate significant differences on the Inhibition-Naming and Speeded Naming subtests when compared to the US norms, however performance still fell within NEPSY-II manual average range. Comparison with the more appropriate SA norms showed that the HIV+ sample performed comparably on measures tapping inhibitory control of automatised responses, and rapid semantic access to names for colours, shapes, sizes, letters, and numbers, but made significantly more errors in the Inhibition-Inhibition subtest. The errors suggest poor strategies/processes used to complete the tasks and do signify some inhibitory control difficulties.

Discussion of Executive Functioning Profile in Relation to the Literature

Significant structural brain changes are evident in children and adolescents living with HIV, including decreases in fractional anisotropy, alongside reductions in cerebral grey matter volumes, cortical surface area, and gyrification, which are associated with poorer cognitive performance (Hoare et al., 2018). The results from the current study reveal notable trends in the effects of HIV infection on neurocognitive functioning in children and adolescents, similar to studies reported in the literature review. Koekkoek et al. (2008) highlighted deficits in EFs among HIV-infected children and adolescents, such as poorer processing speed, pattern recognition, cognitive flexibility, visuospatial memory, and verbal fluency. Additionally, Van Den Hof et al. (2019) found that children and adolescents living with HIV displayed significant decreases in EFs over time compared to controls. Moreover, research emphasises the interconnected nature of EF domains, including updating WM, cognitive flexibility, and inhibitory control, although evidence specific to HIV-infected children and adolescents is limited (Rowe et al., 2021; Walker & Brown, 2018). The subsequent discussion on EF strengths and weaknesses was limited to comparing the HIV+ group's NEPSY-II subtest performance with the SA norms exclusively as it offers the most suitable comparison group. Relying on US-based norms portrays the HIV group as experiencing challenges across all EF domains, despite demonstrating average-range performance on certain subtests when compared to Truter et al. (2017)'s sample. The SA norms provide a more equitable comparison, additionally facilitating the distinction between groups based on age, and thereby allowing for a clearer demonstration of developmental differences. This section compares the cognitive performance of the HIV+ participants across these two distinct age groups: 9–11 and 14–16 years old in relation to the corresponding SA norms for these ages. By shedding light on whether there was a general improvement with age and if specific patterns of similarities and differences emerge within each age cohort, insights were provided into the developmental trajectories and potential areas of vulnerability among HIV+ children and adolescents.

In terms of WM, the comparison between the HIV+ group across age subgroups reveals intriguing patterns of cognitive performance. In the younger cohort (9–11), notable challenges were observed in Auditory Attention and Word List Interference- Repetition, with both measures displaying exceptionally high effect sizes, indicating substantial deviations from SA norms. Conversely, the older cohort (14–16) demonstrated improvement in primary Auditory Attention scores, aligning more closely with the established norms, albeit with significantly higher rates of commission and inhibitory errors. Interestingly, both age groups exhibited comparable performance in Memory for Faces and Word List Interference- Recall, suggesting consistent average proficiency in these areas. However, disparities emerged in delayed memory tasks and word list interference repetition, where the older cohort displayed significantly poorer performance compared to SA norms, indicating potential deterioration or persistence of WM challenges over time.

Consistent with previous research (Milligan & Cockcroft, 2017), these results indicate deficits in WM processing tasks among HIV+ children, particularly in verbal processing. This aligns with the central executive deficit observed in the HIV+ group, as evidenced by their significantly poorer performance on tasks requiring manipulation and processing of information. Similarly, the observed discrepancies in the Word List Interference subtest support the notion of atypical WM organisation, as indicated by Cockcroft & Milligan (2019). These findings appear consistent with the multicomponent WM model proposed by Baddeley et al. (2021), and suggest that deficits in verbal processing tasks among children living with HIV may indicate impairments in the phonological loop, a component of WM responsible for the temporary storage and manipulation of verbal information. Furthermore, discrepancies in the Word List Interference subtest further support the notion of atypical WM organisation, indicating difficulties in suppressing irrelevant information and maintaining focus on relevant stimuli, processes closely associated with the central executive (Baddeley, 2000). Moreover, despite these consistencies, our findings also revealed age-related variations within the HIV+ group. The younger cohort exhibited more pronounced deficits compared to SA norms, whereas the older cohort showed some improvements.

Furthermore, comparing the performance of HIV+ groups across both age ranges on inhibitory control measures indicated various similarities and differences. In the younger cohort (9–11), overall performance aligned comparably with SA norms across the primary measures of all three inhibitory control subtests. However, during the Inhibition-Inhibition subtest the HIV+ group exhibited significantly higher error rates. Similarly, in the older cohort (14–16), performance on primary measures mirrored established norms for South Africans across all three inhibitory control subtests. Yet, like the younger group, a significant increase in errors during the Inhibition-Inhibition subtest was observed. These findings suggest a consistent proficiency in inhibitory control across age groups concerning primary measures, but a specific vulnerability in tasks demanding inhibition of prepotent responses, indicating potential challenges in cognitive flexibility within the HIV+ population regardless of age.

These results suggest generally below-average performance among participants with HIV on measures of inhibitory control, which aligns with the slower processing speed and increased errors in inhibition tasks reported in a previous study by Nichols et al. (2016). Results from that study found that children living with HIV exhibited slower processing speed and increased errors in inhibition tasks compared to their HIV-EU peers (Nichols et al., 2016). Similarly, our study found that children from both age cohorts (9–11 and 14–16) showed increased errors specifically in the Inhibition-Inhibition subtest, despite performing comparably to established norms on primary measures of inhibitory control. This parallel may suggest that inhibitory control deficits, particularly in tasks requiring inhibition of prepotent responses, are a common feature among children and adolescents affected by HIV, potentially irrespective of age or geographical context.

Finally, the comparison of cognitive flexibility task performance between both HIV+ subgroups suggested potential patterns of EF development. While the younger HIV+ cohort exhibited significantly poorer performance on the Response Set subtest compared to SA norms, with notably high effect size, the older group demonstrated comparable performance to the norms. This suggests a potential improvement in cognitive flexibility with age within this population. However, both age groups displayed increased error rates (relative to the norm sample), particularly in Omission Errors for the older cohort, indicating persistent challenges in this regard. Interestingly, while there were no significant differences in the primary measure of the Inhibition-Switching subtest between the groups, both exhibited higher total error rates compared to norms, implying ongoing difficulties. These findings suggest that while cognitive flexibility may improve with age among HIV+ individuals, areas of impairment may persist across adolescence.

Similar to findings from the study by Chongwo et al. (2023), these results indicate that children and adolescents living with HIV exhibited lower cognitive flexibility compared to controls, indicating a consistent pattern of challenges in this domain. For example, HIV-EU children demonstrated stronger cognitive flexibility abilities compared to HIV+ children, indicating that even in the absence of HIV infection, exposure to the virus during prenatal or perinatal stages might still influence neurodevelopment and cognitive outcomes (Chongwo et al., 2023). Similarly, results from this study noted substantial differences between HIV+ children and the control groups on various cognitive flexibility tasks, indicating deficits in cognitive function associated with HIV infection across different age groups. These findings collectively suggest that HIV infection, regardless of age or geographical location, may be associated with cognitive impairments.

As mentioned, the HIV+ groups (cohorts aged 9–11 and 14–16) both performed comparably to the typically developing SA group on some of the subtests tapping inhibitory control (Inhibition-Naming and Speeded Naming), WM (Memory for Faces, and Word List Interference- Recall) and one measure of cognitive flexibility (Inhibition-Switching). This pattern of results may suggest that these cognitive abilities draw on skills that are not significantly affected by HIV. This observation underscores the complexity of HIV-related cognitive impairment and highlights the possibility that certain cognitive domains remain relatively preserved despite HIV infection. Understanding which cognitive functions are resilient to the effects of HIV is crucial for designing interventions and support systems that may help maintain optimal cognitive functioning and quality of life for children and adolescents living with HIV. Further research exploring the specific cognitive mechanisms underlying these abilities could provide valuable insights into protective factors or compensatory mechanisms that mitigate the impact of HIV on cognition.

In conclusion, the comparison of cognitive performance across distinct age groups of HIV+ participants shed light on possible EF developmental patterns and areas of strength or weakness in executive functioning for children and adolescents living with HIV. While improvements with age were evident in certain cognitive domains, challenges persisted, particularly with regards to WM. Nonetheless, certain cognitive functions appeared resilient to the effects of HIV, highlighting the possibility of protective factors or compensatory mechanisms. The use of appropriate norms (i.e. those derived from typically developing South African children) was able to identify these resilient cognitive functions, whereas comparison against the US norms typically indicated that children living with HIV performed significantly poorer in most areas of cognitive function. The findings presented in this section underscore the significant impact of HIV infection on neurocognitive functioning in children and adolescents. The utilisation of appropriate and representative norms was imperative for determining cognitive profiles that effectively gauge a child's performance relative to their typically developing peers, as this ensures accurate and fair assessments, ultimately guiding tailored interventions and support strategies. Moreover, segregating performance by age facilitates the identification of developmental patterns and milestones. Additionally, exploring error patterns on the NEPSY-II subtests provides invaluable insights into cognitive processes and strategies employed during tasks, which is obscured when looking only at the overall accuracy score. For instance, error scores for children and adolescences living with HIV reveal discernible differences in strategy utilisation compared to their typically developing peers, indicating potentially haphazard approaches that may hinder task performance. Specifically, through the examination of various EF domains (WM, inhibitory control, and cognitive flexibility) consistent challenges have been observed among young people living with HIV compared to their uninfected peers.

These findings corroborate existing literature, emphasising the pervasive nature of cognitive impairment associated with HIV infection, even in cases of cART use, across various age groups and contexts. Ultimately, these insights not only contribute to the overarching understanding of the neuropathological effects of HIV but also have significant implications for the design of tailored interventions aimed at optimising cognitive outcomes in this vulnerable population. Now that a workable EF profile for children and adolescents living with HIV has been established based on data available for a cohort of South African children, the third research question was discussed. The following section examined patterns and correlations between BRIEF and NEPSY-II subtests, interpreting them in light of available literature.

Correlations Between BRIEF and NEPSY-II Subtests

The third research question explored whether the BRIEF and NEPSY-II measures tap similar or different EFs in the study sample. These correlations can be summarised as follows: Specifically, stronger WM as measured by the BRIEF was associated with stronger WM as measured by the NEPSY-II subtests. Furthermore, the good performance on the BRIEF'S BRI (which is a measure of a child's ability to regulate their behaviour, and includes aspects such as inhibition, shifting, and emotional control) is associated with stronger WM, as measured by the NEPSY-II subtest WI Repetition. Additionally, better performance on both NEPSY-II inhibitory control and WM tasks are associated with lower (better) MI scores on the BRIEF, which taps into how well a child can effectively plan, organise, and execute tasks, as well as their ability to self-monitor and adapt strategies when needed (Gioia et al., 2000). Specifically, these results reveal significant associations between raw scores on the BRIEF and NEPSY-II measures, indicating convergent validity between these assessment tools (despite the difficulties identified, and discussed earlier, with the BRIEF scores). This parallels the significant correlations found in studies with young boys between the age of 8–11 years (Shimoni et al., 2012) and adolescents between the ages of 13–18 years (Toplak et al., 2008), which also demonstrated alignment between cognitive and behavioural measures of EF in specific domains. For instance, this study identified associations between BRIEF WM scales and corresponding NEPSY-II WM subtests, supporting the notion that these measures tap similar EF constructs (Toplak et al., 2008). The CEN, which is compromised in HIV, plays a crucial role in coordinating complex cognitive processes, including EFs, as well as various behavioural functions (Ipser et al., 2015; Nolan & Gaskill, 2019; Shen et al., 2020). As such, the compromised CEN in children and adolescents living with HIV may be influencing the relationship between EF measures such as the BRIEF and NEPSY-II and their respective cognitive and behavioural outcomes. Furthermore, the negative correlation between BRIEF MI and BRI scores and NEPSY-II tasks for inhibitory control and WM is consistent with findings suggesting that deficits in cognitive control are reflected in behavioural ratings of EF (Shimoni et al., 2012). Overall, these results contribute to the body of evidence suggesting that while cognitive and behavioural measures of EF may not always align perfectly, there is substantial overlap in the constructs they assess, supporting the multidimensional nature of EF.

Furthermore, in terms of which NEPSY-II subtests correlate with each other, results suggest a pattern of interrelatedness among specific NEPSY-II subtests, shedding light on the underlying cognitive processes. Subtests measuring WM (Auditory Attention, Memory for Faces, Word List Interference Recall and Word List Interference Repetition) were all significantly inter-correlated. Similarly, measures of cognitive flexibility (Response Set and Inhibition-Switching) were significantly correlated, as were measures of inhibitory control (Inhibition-Naming, Inhibition-Inhibition and Speeded naming). With regards to the BRIEF, all included scales (Inhibit, Shift, Working Memory, BRI, MI, and GEC) were positively and significantly correlated with one another, indicating a cohesive pattern of EFs. The strongest correlations were observed between BRI and GEC, as well as between MI and GEC, which is understandable as the GEC is comprised of the BRI and MI. The interconnectedness of these subtests with one another underscores the holistic nature of executive functioning and highlights the importance of considering multiple facets when assessing and interpreting EF abilities.

Research Implications

Limitations and General Reflections

There were several limitations to this study. Firstly, the research design was non-experimental and exploratory in nature, and as such, no assumptions can be made regarding causality between variables (Verma, 2019). A second potential limitation of this study is the administration of EF subtests in English, while most of the participants spoke predominately isiXhosa, isiZulu and, less so, Afrikaans. Being tested in a language other than one's mother tongue may reduce comprehension, exaggerating potential cognitive burdens associated with language processing. However, in the multilinguistic context of South Africa, accommodating all languages is not always feasible. Additionally, this study utilised secondary data. This brings with it disadvantages, such as confidentiality measures leading to the omission of identifying variables, potentially introducing confounding factors unknown to the researcher. Moreover, the use of secondary data introduces a disconnect between data analysts and original data collectors which may lead to details crucial for interpretation being overlooked (Cheng & Phillips, 2014). However, in this case that concern was mitigated as the primary researcher was a co-supervisor for this study. On the other hand, the secondary analysis of existing data offers several advantages, notably its cost-effectiveness, particularly benefiting graduate students and researchers with limited resources. Moreover, it encourages innovative cross-linking of information, facilitating novel research approaches (Cheng & Phillips, 2014).

Another major limitation in the interpretation of the results is the high number of missing responses and low raw scores for the BRIEF subtests resulting in a lack of variation in the standardisation of the scores. This raises questions regarding the viability of the BRIEF as a reliable measure of executive functioning, particularly in populations affected by conditions such as HIV. The presence of missing responses and low scores may indicate potential challenges in the applicability and sensitivity of the BRIEF within this context. These findings underscore the necessity for a critical re-evaluation of the BRIEF's efficacy within this demographic, prompting further investigation into alternative assessment methods or modifications to enhance assessment of EFs in paediatric HIV populations. Additionally, considering the potential time constraints and cognitive challenges faced by paediatric patients, future research might explore the utility of the shorter version of the BRIEF. The short version generally displayed suitable psychometric properties, supported by evidence for the reliability and validity of the BRI, MI, and GEC (LeJeune et al., 2010). Investigating the applicability and effectiveness of these abbreviated versions specific to the SA paediatric context could provide valuable insights into streamlining assessment procedures while maintaining diagnostic accuracy in atypically developing population.

Furthermore, while efforts were made to compare EF performance against appropriate normative samples, including those specific to the SA population, discrepancies in cultural and socio-economic backgrounds between the study sample and normative groups may have impacted the validity of the comparisons. Lastly, the use of caregiver-reported measures, such as the BRIEF, may have introduced subjectivity and potential biases, which, in turn, may have affected the accuracy EF performance. This is unfortunately the general problem with subjective assessment measures such as the BRIEF (Hess et al., 2020). Despite these limitations, the study provided insights into the EF challenges experienced by children and adolescents living with HIV, laying the groundwork for future research in this under-explored area.

Study Contributions and Recommendations for Future Research

Despite its limitations, a major contribution of this study is that it highlights and contributes to a dearth of research surrounding our understanding of executive functioning in atypical populations. By delineating specific cognitive profiles and highlighting discrepancies in WM, cognitive flexibility, and inhibitory control compared to normative data, this study underscored the impact of HIV on EFs, particularly in the context of South Africa. Additionally, this study makes a significant contribution by emphasising the importance of utilising appropriate norms for valid comparisons, particularly within South Africa's unique multicultural, socio-economic context. While South Africa faces economic constraints that prevent the collection of large-scale norms, the utilisation of smaller comparison groups, as done by Truter et al. (2017), offers a viable alternative. In acknowledgment of the challenge a lack of representative norms poses to neuropsychological assessment in South Africa, Ferreira-Correia and Cockcroft (2023) propose the adoption of Crawford and Howell's Single-Case Methodology in Neuropsychology as a viable solution for cases not adequately covered by existing norms. This methodology involves comparing the scores of individual cases to those of a carefully matched sample of modest size. To facilitate its implementation, a set of norms specifically tailored to South Africans with diverse demographic profiles is provided, covering a range of well-established neuropsychological tests (Ferreira-Correia & Cockcroft, 2023). This recommendation underscores the importance of developing contextually relevant assessment tools and methodologies to enhance the validity and applicability of neuropsychological evaluations in diverse settings. Future research should explore the effectiveness and broader implications of implementing such tailored approaches in clinical practice and research within South Africa.

Moreover, the identification of age-related patterns suggests potential developmental trajectories of EF within HIV-positive cohorts. Future research in this area could benefit from employing longitudinal ex-post-facto designs, both to explore these possible developmental trajectories and to attempt to establish causal relationships between HIV infection and EF deficits. Additional recommendations for future research include investigations into protective factors or compensatory mechanisms that may mitigate HIV-related cognitive deficits, and studies examining the interplay between HIV infection, socioeconomic factors, and access to healthcare, which could provide valuable insights into the multifaceted nature of EFs in this population.

Furthermore, efforts to expand the study's sample size and diversify participant demographics could enhance the generalisability of findings and provide a more comprehensive understanding of EF disparities among young people living with HIV. Moreover, incorporating qualitative methodologies, such as interviews or focus groups, could offer deeper insights into the subjective experiences of HIV+ youth and their caregivers, informing more holistic approaches for both assessment and intervention, and tap into the characteristics of self/guardian-reported measures such as the BRIEF. Finally, efforts to develop and validate culturally appropriate assessment measures for EF in diverse populations are needed. Overall, while the study provides valuable preliminary findings, continued efforts to address its limitations and build upon its insights will be crucial for advancing knowledge in this area and, ultimately, informing interventions to support children and adolescents living with HIV.

Conclusion

This study has provided valuable insights into the EF challenges faced by children and adolescents living with HIV in South Africa. By examining specific domains of EF, such as WM, inhibitory control, and cognitive flexibility, the study aimed to understand the neurocognitive impact of HIV infection in paediatric populations. In line with challenges associated with assessing EF in children, the study attempted to utilise both cognitive measures (NEPSY-II) and behavioural rating scales (BRIEF) to comprehensively evaluate EF performance. However, methodological issues with the BRIEF prevented accurate standardisation of the scores and thus they were excluded from interpretation. Statistical analysis revealed significant discrepancies in WM, cognitive flexibility, and inhibitory control between HIV-positive participants and normative samples, aligning with existing literature highlighting EF challenges in HIV-infected children and adolescents. Moreover, age-related variations within the HIV-positive group were noted, suggesting potential developmental trajectories of EF within this population. Importantly, the identified challenges in EFs facing children and adolescents living with HIV underscore the pressing need for targeted remediation approaches and interventions. Executive functioning skills are fundamental for academic achievement, social interactions, and overall adaptive functioning

(Anabwani et al., 2016). As such, addressing these challenges early on may significantly enhance the quality of life and long-term outcomes for HIV-positive youth. Interventions tailored to improve EF abilities, such as cognitive training programs and educational support strategies, should be developed and implemented within healthcare and educational settings. Additionally, fostering a supportive environment that accommodates the unique needs of HIV-infected children and adolescents, including access to mental health services and educational accommodations, is imperative.

Through correlations between BRIEF and NEPSY-II measures, the study revealed significant associations, indicating convergent validity between these assessment tools. Furthermore, the interrelatedness among specific NEPSY-II subtests and BRIEF subtests underscored the holistic nature of EF and emphasised the importance of considering multiple facets when assessing and interpreting EF abilities. These findings not only contribute to our understanding of EF in atypical populations but also have significant implications for the design of tailored interventions aimed at optimising cognitive outcomes in children and adolescents living with HIV. Overall, the study provided valuable insights into the intricate interplay between HIV infection and cognitive functioning in children and adolescents, laying the groundwork for future research and interventions aimed at supporting cognitive well-being.

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Zondo, S. (2021). *Customised Cognitive Rehabilitation for a paediatric HIV/AIDS population corroborated by fNIRS: The case of Sustained Attention (Research Proposal)* [PhD Research Proposal]. University of Witswatersrand.

Appendix A

Demographic Questionnaire

Your name:	Date:
Child's Name:	School:
Age of Child:	Date of Birth
Name of Shelter	

1. Child's Sex: (circle one):	**Male**	**Female**	
2. Child's Grade:			
3. Home language: (circle one):	isiZulu	isiXhosa	Other
4. Handedness (circle one):	Left	Right	Ambidextrous
5. Who is the primary caregiver of the child?			
6. What is your relationship to the child? (circle one):	Mother	Father	Guardian
7. Has your child been diagnosed with HIV? (circle one):	Yes	No	
8. Is your child on ARVs?	Yes	No	

9. Does your child take part in regular activities such as reading and math? If yes, please specify as well as describe the regularity of these activities?	
10. How would you describe your child's personality?	

11. Does your child have a history of any of the following?

(a) **Neurological disorder**: Has your child been diagnosed with any diseases of the brain, spine or nerves?

Yes ☐ No ☐

If Yes please specify____

(b) **Traumatic brain injury**: Has your child ever suffered a major blow to the head that left them unconscious for more than 30minutes?

Yes ☐ No ☐

If Yes please specify____

(c) **Psychiatric disorders**: Has your child shown any pattern of behavior that seemed abnormal/atypical which led to seeking help at a mental hospital?

Yes ☐ No ☐

If Yes please specify____

(d) **History of pre-natal or birth complications**: Were there any complications during pregnancy (did the pregnancy take the normal 9months) or complicated delivery (e.g. was the child pulled out using forceps)?

Yes ☐ No ☐

If Yes please
specify____

(e) **History of learning disability or special education**: Has your child ever had any difficulty with learning concepts, to a point where s/he ended up needing special classes?

Yes ☐ No ☐

If Yes please
specify____

(f) **Two or more repeated grades**: Has your child ever had to repeat any grades at school?

Yes ☐ No ☐

If Yes please
specify____

(g) **The use of psychotropic medication:** Has your child ever taken medication that changes their mood or behavior?

Yes ☐ No ☐

If Yes please
specify____

Appendix B

Ethical Clearance Certificate for Mr Sizwe Zondo

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Mr Sizwe Zondo

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M211073

NAME: (**Principal Investigator**) Mr Sizwe Zondo

DEPARTMENT: School of Human and Community Development: Psychology
Nkosi's Haven in Johannesburg
The Home of Joy in Grahamstown / Makhanda

PROJECT TITLE: Cognitive Rehabilitation for a paediatric HIV/AIDS population: The case of Sustained Attention

DATE CONSIDERED: 29/10/2021

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Prof K. Cockcroft and Dr A. Ferreira-Correia

APPROVED BY: CB Penny
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 09/12/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore be due in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

09/25/21
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix C

Letter To The Director Of HIV Shelter- Request To Conduct Research on Premises

Dear Director,

I am a PhD Psychology student and a member of the University of Witwatersrand's Neuroscience Research Laboratory (https://www.witsneurl.com/). For my research, I am interested in investigating cognitive difficulties that result from the Human Immunodeficiency Virus (HIV). Recent research indicates that despite advances in the management of HIV infection through the use of antiretroviral drugs (ARTs), children living with HIV continue to experience what is referred to as: HIV-Associated Neurocognitive Decline (HAND). This cognitive decline is thought to result from HIV entering the brain, and affecting brain functions, that lead to children experiencing difficulty paying attention, and creating long-term memories. For my research, I am interested in investigating brain plasticity and how brain training exercises can help reverse some of the decline experienced by children living with HIV.

Who can participate?

I am looking to recruit children at your shelter, between the ages of 7 and 16 years of age, living with HIV. In addition to your consideration, children will be asked to provide assent to participant in the study and will be informed that they are free to withdraw from the study at any point, without being penalised in any way.

What will happen during the study?

For the study, children will complete a number of tasks. Firstly, children will be requested to complete cognitive tasks that aim to assess attention skills. The cognitive tasks will be based on two instruments called the NEPSY-II, and the Conner's Continuous Performance Test (CPT). Children will complete these cognitive tasks, before and after the brain training exercises. The brain training exercises will be computerized and designed to specifically train attention skills. Each child who takes part in the study will be trained independently, by the researcher and his research assistant. Lastly, to investigate the benefits of the brain training exercises on children's attention skills, I will assess children's brain activity using a safe, non-invasive instrument called, functional near-infrared spectrometry (fNIRS). fNIRS is a neuroimaging technique that indicates hemodynamic (blood) responses due to brain activity. The data from fNIRS is obtained by using light sources and detectors that are placed on the children's scalp. The light sources and detectors indicate how much oxygenated blood haemoglobin is absorbed in the brain during a cognitive task. The more light is absorbed, the more active the brain region of interest. This procedure of brain analysis is commonly used paediatric research with children living in Africa (e.g. Grazioli et al, 2019).

Duration of the Study and Role of Children:

All children will be assessed at the beginning of the study, immediately following the brain training exercises, and 6 months after completing the brain training exercises. All in all, the study will last for a duration of about 6 months. The brain training exercises will be completed at least three times per week, for about 30 minutes per session. Each child will receive 24 brain training sessions, over a 3 month period using a training program known as the Computerised Progressive Attentional Training program (CPAT) (Shalev et al., 2007).

What will happen to the findings from the study:

All findings from the study will be kept confidential. If any data from the study is published, all identifying information such as the children's identity or the organisation's identity will be kept private. Moreover, all results emanating from the study will be shared with you as soon as they are available.

Who has approved this study?

This study has received ethical approval from the University of the Witwatersrand's Human Research Ethics (Medical) Committee.

Who is responsible for this study?

I the Doctoral Candidate (Sizwe Zondo) who is conducting the study is responsible for the study, and can be contacted at any time with any queries. My supervisors, Dr Ferreira-Correia and Professor Cockcroft can also be contacted if you have any queries or complaints regarding the research and any associated risks. All contact details are included at the end of this letter.

Thank you for your time and consideration.

Should the above be to your satisfaction, and you provide consent for me to conduct research at your shelter, may you kindly append your signature to the below designation.

………………………………………..

Signature: Director

Mr. Sizwe Zondo	Dr Aline Ferreira-Correia	Professor Kate Cockcroft
PhD Psychology Candidate	Senior Lecturer	Associate Professor
Department of Psychology	Department of Psychology	Department of Psychology
Rhodes University	University of the Witwatersrand	University of the Witwatersrand
076478146/ 046-603-8503	0117174527	+27117174511
S.Zondo@ru.ac.za	Aline.FerreiraCorreia@wits.ac.za	Kate.Cockcroft@wits.ac.za

Appendix D

Information Letter To Parent/Guardian Regarding Child Participation In Research

Dear Parent/Guardian

I am a Ph.D. student at the University of Witwatersrand, based in the Department of Psychology. For my Ph.D. research, I am investigating the effects of the Human Immunodeficiency Virus (HIV) on children's thinking abilities. I am particularly interested in exploring how a key component of our thinking, called 'sustained attention,' is affected in children living with HIV. Moreover, I am interested in investigating whether specific brain exercises can help improve children's attention skills. To achieve my research goals, I intend to recruit participants aged between the ages of 7 and 16 years of age to take part in the research study. With the help of the Director at (name of children's home) and with your consent, I kindly request the participation of your child in my research. For the research, all children will be tested independently in a room located at the children's home where your child resides. Children will complete a number of tasks, including (a) psychological measures to assess for attention, (b) complete computer-based brain training exercises, and (c) undertake neuroimaging sessions to investigate the results of the brain training exercises.

All the above techniques will be administered by a researcher who is trained in the administration of these tasks. All psychological measures will be done at the beginning of the study, immediately following the brain training exercises, and 6 months after the children complete the brain training exercises. The average time to complete the psychological measures will be roughly 45 minutes. (b) The computer brain training exercises include tasks to train attention skills amongst participants. The brain training exercises will be completed at least three times per week, for about 30 minutes per session. In total, children will receive approximately 24 brain training exercise sessions, over a 3 month period, using the Computerised Progressive Attentional-Training program (CPAT) (Shalev et al., 2007).

(c) Lastly, to investigate the benefits of the brain training exercises on children's attention skills, your child's brain activity will be assessed using a safe, non-invasive instrument called functional near-infrared spectrometry (fNIRS). This imaging technique allows us to study hemodynamic (blood) responses in children's brains as they respond to brain training. We acquire the imaging data by using light sources and detectors that are placed on the children's scalp. The light sources and detectors indicate how much oxygenated blood is absorbed by haemoglobin (a protein in blood) in the brain, during the attention tasks, before and after the brain training. All in all, children will be assessed for attention at the beginning of the study, immediately following the brain training exercises, and 6 months after completing the brain training exercises.

My research does not envisage any risks or harm to your child. Participation in the study will be voluntary, and your child will be able to withdraw from the study at any point. Moreover, your child's name or other identifying details will not be used at any point during the study to identify their participation in the research. Should you have any questions, please do not hesitate to contact me or my research supervisors, Dr. Ferreira-Correia and/or Professor Cockcroft, for any queries or complaints regarding the research. All contact details are included below.

Thank you for your time and consideration.

Should the above be to your satisfaction, please read and complete the 'Informed Consent' form below.

Yours Sincerely,

Student Researcher	Research Supervisor	Research Supervisor
Mr. Sizwe Zondo	Dr Aline Ferreira-Correia	Professor Kate Cockcroft
Ph.D. Psychology Candidate	Senior Lecturer	Associate Professor
Department of Psychology	Department of Psychology	Department of Psychology
Rhodes University	University of the Witwatersrand	University of the Witwatersrand
076478146/ 046-603-8503	0117174527	+27117174511
S.Zondo@ru.ac.za	Aline.FerreiraCorreia@wits.ac.za	Kate.Cockcroft@wits.ac.za

Appendix E

Informed Consent Form for Parents/Guardian of HIV+ Children Living at the Shelter

The study has been explained to me, and my questions have been answered. I have understood that participation in this study is voluntary and that I may withdraw my child at any point. I understand that my child will not be identified except by an initial and that this anonymity will be maintained throughout the study and when the research is published.

I consent to participate and to allow my child to **participate** in this study

Child's Name	
Signature of Parent/Guardian	
Date	

I hereby give consent for cognitive data to be collected from my child in order to for the researchers to analyse attention skills in my child. I understand that cognitive function data will be acquired using psychological instruments that assess attention and psychological skills. I also provide consent for my child to undertake the brain training exercises to remediate attention skills. I also provide consent for fNIRS neuroimaging to be used to collect blood hemodynamic responses related to brain activity in my child. I understand that fNIRS neuroimaging is a safe, and non-invasive, technique used for research purposes, and I provide consent for data emanating from the use of this imaging technique to be stored at the Department of Psychology, at Wits University, or at Rhodes University for research purposes.

Signature of Parent/Guardian	
Signature of Researcher	
Date	

{Parent/guardian}**____**has been informed of the purpose, procedures, and any possible risks of this study. He/she has been given time to ask any questions, and these questions have been answered to the best of my ability. He/she understands that participation is voluntary.

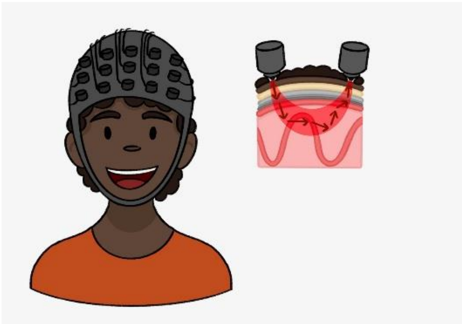
Researcher	
Signature & Date	

Appendix F

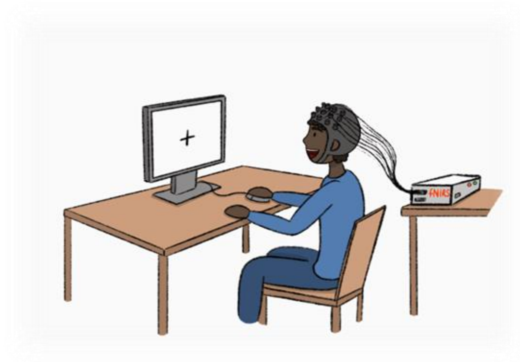
Assent Form: Collection of Psychological and Neuroimaging Data

Good day! I would like to tell you about a research study that I am doing. A research study allows us to learn about the world. In this research study, we want to learn more about how your brain works.

If you join this study, I will ask you to wear something that looks like a cap around your head. This cap will not hurt you at all. You can see how the cap looks from the picture below. You might be asking yourself, how does the cap work? Let me explain. Have you ever been in a dark room, and someone shined a light into the room for you to see where you were? The cap does the same thing. It has a place that shines light into your brain. It also has a place that collects the shined light. In the picture below you can see two knobs. One knob represents the light that we shine into your head, the other knob represents the light that is collected on the other side. The small arrows show the direction of the light as it travels through your brain. We want to know how much of the shined light as taken up by your brains and how much as collected back, as you do various thinking task.



During the study, I will ask you to complete some tasks and play a few games with me. In one of the games, you will look into a computer screen, sometimes you will see letters (A, B), and sometimes you will see an '+' sign like you can see below. Some of the games will involve looking at pictures with me. I will ask to see you often as I train you to improve on the above games. Every time we meet we will have new training tasks on a computer, and you will get better at the game. If you get tired, then we can take a break.



You do not have to join this study if you do now want to. It is also fine if you join the study, but change your mind to say you want to stop.

Do you have any questions?

{Participant's name} _______________ has been informed of the purpose, procedures, and possible risks of this study. S/he has also been granted the opportunity to ask questions, and all the questions have been answered to the best of my ability. The participant understands that participation in the study is completely voluntary.

Researcher	
Signature & Date	

Appendix G

Data Permission Request

Dear Nike Mes (719430)

SUBJECT: Permission to Receive Data

This letter serves as an acknowledgement of your request to receive the anonymised data from the BRIEF and NEPSY-II assessments collected from 42 participants in the "Customised Cognitive Rehabilitation for a paediatric HIV/AIDS population corroborated by fNIRS: The case of Sustained Attention" research study. This database was requested for use in your master's thesis, titled 'Executive Functioning in a HIV-Positive Paediatric Population'. The following restrictions apply to scope of study, participant protection protocol, and data extent usage.

<u>Scope of the Study</u>

The research project, 'Executive Functioning in a HIV-Positive Paediatric Population', is supervised by Professor Kate Cockcroft and Mr Sizwe Zondo. The aim of this proposed study is to use the requested secondary data in order to compare executive functioning (EFs) of children and adolescents with HIV-Associated Neurocognitive Disorder (HAND) to that of typically developing peers. To determine which EFs are affected, a comparison with the control will identify areas where children living with HIV perform significantly poorer or comparable on two measures of EF, namely the A Developmental Neuropsychological Assessment (NEPSY-II) and the Behaviour Rating Inventory of Executive Function (BRIEF). Additionally, this study will aim to explore the intercorrelations between the participants' scores on the NEPSY-II subtest and the BRIEF to determine whether the measures tap similar or separate EFs.

This study will be directed by three key research questions:

1. Do HIV+ South African children with HAND show compromised executive function compared to those of a typically developing paediatric population?
2. Specifically, which executive functions are affected in HIV+ South African children living with HAND?
3. To what extent does the parent/teacher rating on the BRIEF correlate with the NEPSY-II scores? (Do the BRIEF and NEPSY-II measures tap similar or different EFs)

<u>Participant Protection Protocol</u>

This section serves to outline the protocol used to protect the participant's data, anonymity and confidentiality. As you are requesting an anonymous database, and no identifying information regarding the setting or participants will be provided in the data analysis or write-up of the study, the anonymity and confidentiality of the participants will be ensured. Furthermore, the data will not be shared with anyone without the expressed, written permission of both Mr Zondo and his supervisors. Finally, the data will be stored on a password-protected computer with restricted access. If the data is transported, it will first be encrypted and password protected first.

<u>Data Usage Extent</u>

This letter serves as permission for the data to be used in the research project 'Executive Functioning in a HIV-Positive Paediatric Population' towards the research report of Nike Mes' Masters in Social and Psychological Research at the University of the Witwatersrand, 2023-2024. If the results prove to be publishable, this may be considered in discussion with ourselves, who would be co-authors on the publication.

If you require any further information or clarification, do not hesitate to contact us.
Kind Regards,

Signature: Signature: Signature:

Mr. Sizwe Zondo	Dr Aline Ferreira-Correia	Professor Kate Cockcroft
PhD Candidate	Senior Lecturer	Professor
Department of Psychology	Department of Psychology	Department of Psychology
Rhodes University	University of the Witwatersrand	University of the Witwatersrand
076478146/ 046-603-8503	0117174527	+27117174511
S.Zondo@ru.ac.za	Aline.FerreiraCorreia@wits.ac.za	Kate.Cockcroft@wits.ac.za

Appendix H

Ethical Clearance Certificate for Ms Nike Mes

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

SCHOOL OF HUMAN AND COMMUNITY DEVELOPMENT ETHICS COMMITTEE
CONSTITUTED UNDER THE UNIVERSITY HUMAN RESEARCH ETHICS COMMITTEE (NON-MEDICAL)

CLEARANCE CERTIFICATE **PROTOCOL NUMBER: MAPSYC/23/07W**

PROJECT TITLE: Executive Functioning in a HIV-positive Paediatric Population.

INVESTIGATOR Mes Nike Francis (719430)

SCHOOL/DEPARTMENT OF INVESTIGATOR SHCD/Psychology

DATE CONSIDERED 14 June 2023

DECISION OF THE COMMITTEE Approved unconditionally

RISK LEVEL No Risk

EXPIRY DATE 31 December 2025

ISSUE DATE OF CERTIFICATE 03 June 2023 **CHAIRPERSON** ____________________
(Dr Aline Ferreira Correia)

cc: Prof. Kate Cockcroft (Supervisor)

DECLARATION OF INVESTIGATOR

To be completed in duplicate and **ONE COPY** returned to the Chairperson of the School/Department ethics committee.

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 be contemplated from the research procedure as approved, I/we undertake to submit an amendment of the protocol to the Committee.

____
Signature

Date 12 / 07 / 2023

PLEASE QUOTE THE PROTOCOL NUMBER ON ALL ENQUIRIES

Appendix I

Data Management

Table I 1

Dependent Variable Descriptions

Variable	Test	Description	Standardised Score
Auditory Attention	NEPSY-II		
AA Total Correct		Primary Score	Scaled Score (Ages 6-12) Percentile Rank (Ages 13-16)
AA Commission Errors			Percentile Rank
AA Omission Errors			Percentile Rank
AA Inhibitory Errors			Percentile Rank
Response Set	NEPSY-II		
RS Total Correct		Primary Score	Scaled Score (Ages 6-12) Percentile Rank (Ages 13-16)
RS Commission Errors			Percentile Rank
RS Omission Errors			Percentile Rank
RS Inhibitory Errors			Percentile Rank
Inhibition-Naming	NEPSY-II		
INN Total Errors			Percentile Rank
INN Total Completion		Primary Score	Scaled Score
Inhibition-Inhibition	NEPSY-II		
INI Total Errors			Percentile Rank
INI Total Completion		Primary Score	Scaled Score
Inhibition-Switching	NEPSY-II		
INS Total Errors			Percentile Rank
INS Total Completion		Primary Score	Scaled Score
Memory for Faces	NEPSY-II		
MF Total Score		Primary Score	Scaled Score
Memory for Faces Delayed	NEPSY-II		
MFD Total Score		Primary Score	Scaled Score
Word List Interference	NEPSY-II		
WI Repetition		Primary Score	Scaled Score
WI Recall		Primary Score	Scaled Score
Speeded Naming	NEPSY-II		
SN Completion Time		Primary Score	Scaled Score

SN Total Correct			Percentile Rank
SN Total Self-Corrected			Percentile Rank
Inhibit	BRIEF	BRI subtest; Primary Score	T Scores and Percentile Rank
Shift	BRIEF	BRI subtest; Primary Score	T Scores and Percentile Rank
Working Memory	BRIEF	MI subtest; Primary Score	T Scores and Percentile Rank
Behavioural Regulation Index	BRIEF	Primary Score	T Scores and Percentile Rank
Metacognition Index	BRIEF	Primary Score	T Scores and Percentile Rank
Global Executive Composite	BRIEF	Primary Score	T Scores and Percentile Rank

Appendix J

Normality Outputs

Table J 1

Normality Statistics of Primary Scores for subtests from the NEPSY-II and BRIEF

Variable	Skewness	Kurtosis	Shapiro-Wilk
AA Total Correct	-0.785	-0.596	0.866*
AA Commission Errors	2.193	6.920	0.791*
AA Omission Errors	0.699	-0.784	0.874*
AA Inhibitory Errors	-0.570	-1.202	0.858*
RS Total Correct	-0.837	-0.488	0.881*
RS Commission Errors	2.266	4.651	0.604*
RS Omission Errors	0.934	-0.139	0.883*
RS Inhibitory Errors	0.938	0.374	0.715*
INN Total Errors	4.860	25.353	0.356*
INN Total Completion	4.102	21.618	0.560*
INI Total Errors	2.024	4.460	0.781*
INI Total Completion	2.488	9.566	0.784*
INS Total Errors	0.373	-0.877	0.938*
INS Total Completion	2.027	5.827	0.827*
Memory for Faces	0.216	-0.829	0.950
Memory for Faces Delayed	-0.339	-0.182	0.964
Word List Interference- Repetition	0.662	-0.137	0.949
Word List Interference- Recall	0.325	0.082	0.977
SN Completion Time	4.122	21.036	0.586*
SN Total Correct	-1.733	3.418	0.728*
SN Total Self-Corrected	0.717	-0.617	0.844*
Brief Inhibit	-.0151	4.286	0.819*

Brief Shift	0.752	1.324	0.905*
Brief Working Memory	-0.280	0.996	0.933*
Behavioural Regulation Index	0.656	3.684	0.827*
Metacognition Index	1.538	6.714	0.810*
Global Executive Composite	0.894	5.960	0.839*

Notes. *$p \leq .05$.

Figure 1

Distribution Pattern of AA Total Correct (n = 40)

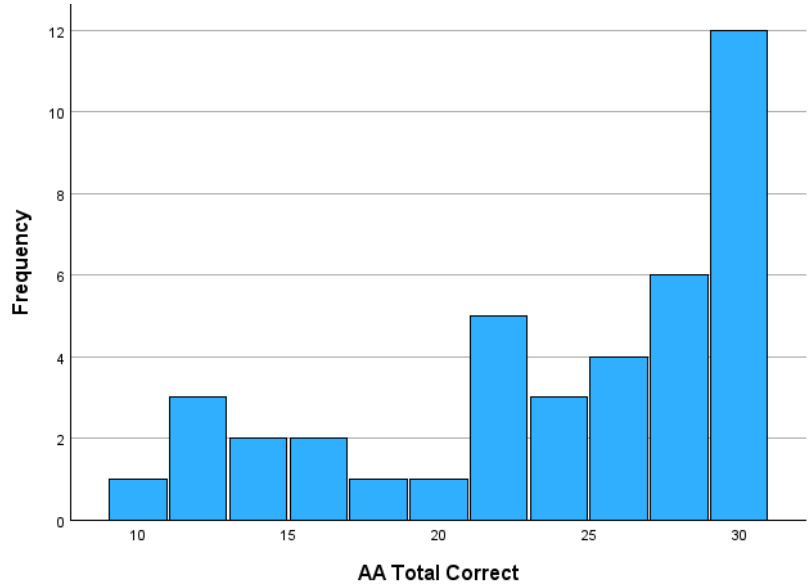


Figure 2

Distribution Pattern of AA Commission Errors (n = 40)

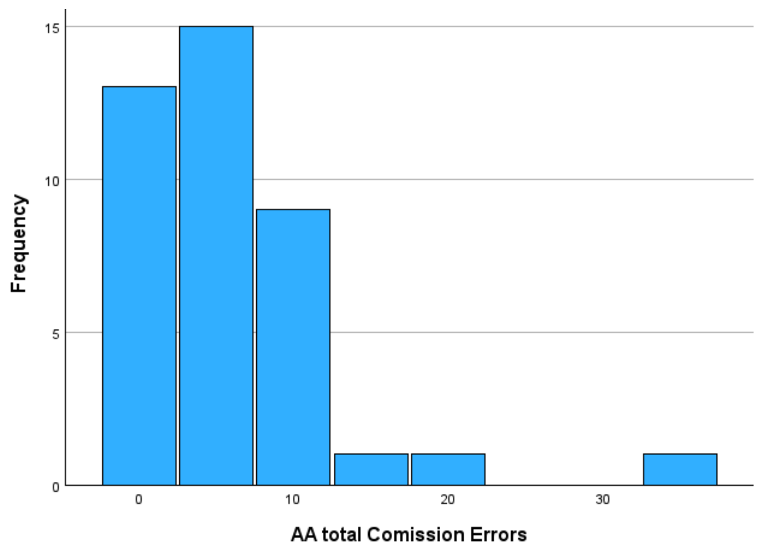


Figure 3

Distribution Pattern of AA Ommission Errors (n = 40)

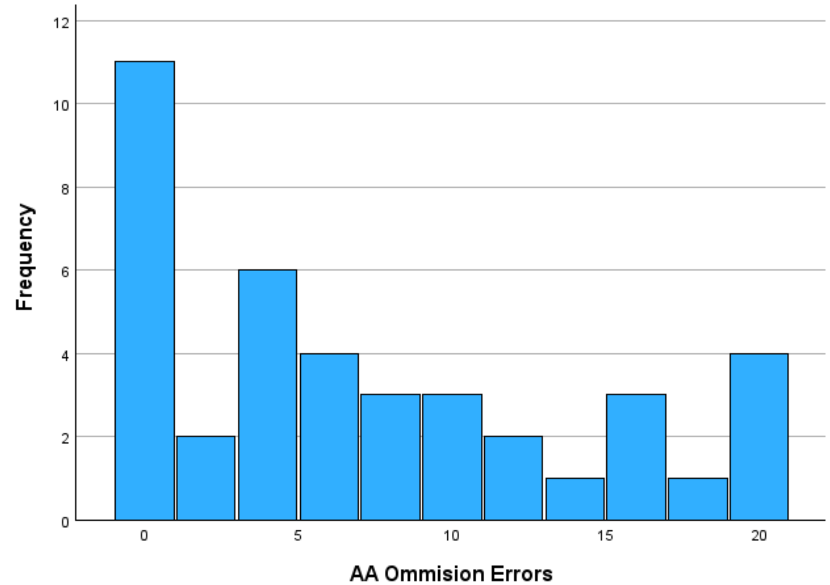


Figure 4

Distribution Pattern of AA Inhibitory Errors (n = 40)

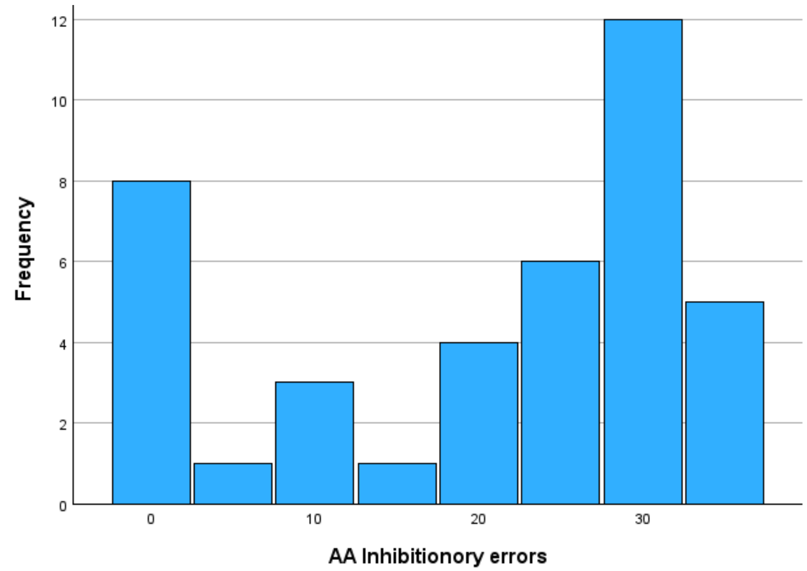


Figure 5

Distribution Pattern of RS Total Correct (n = 40)

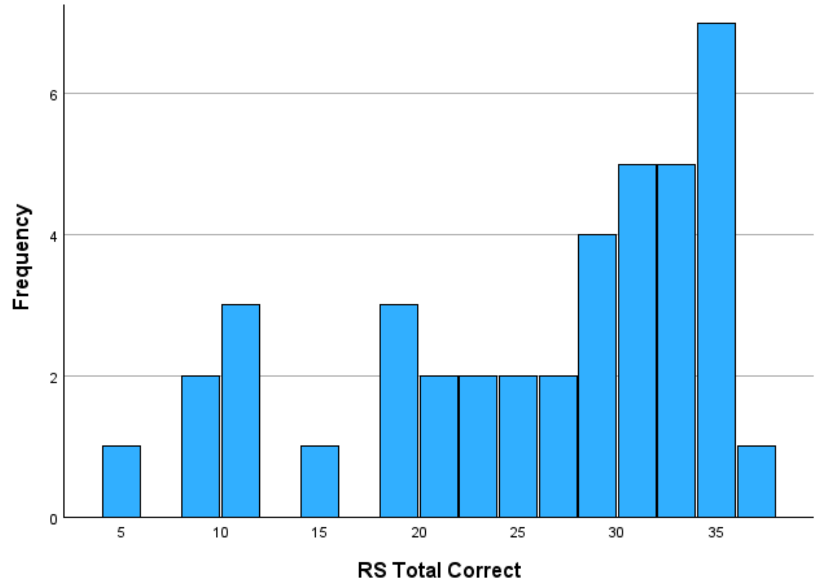


Figure 6

Distribution Pattern of RS Commission Errors (n = 40)

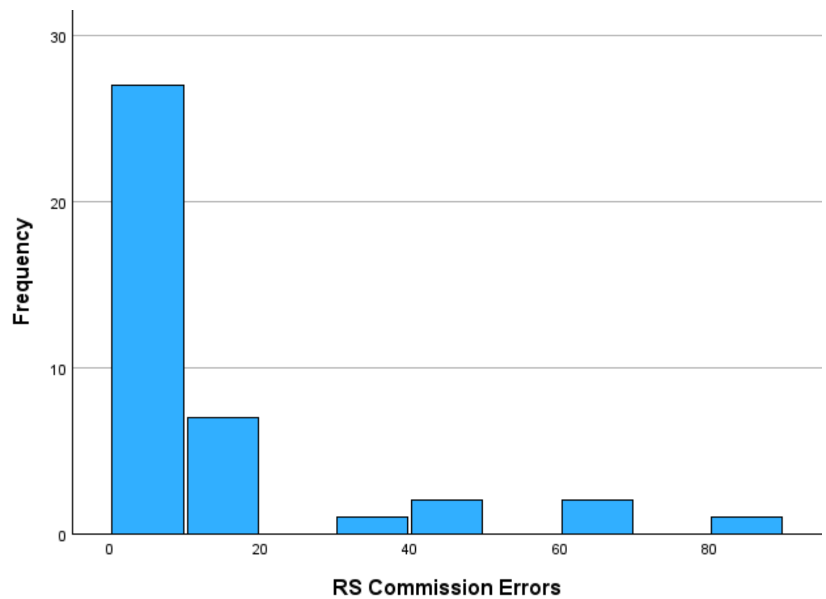


Figure 7

Distribution Pattern of RS Ommission Errors (n = 40)

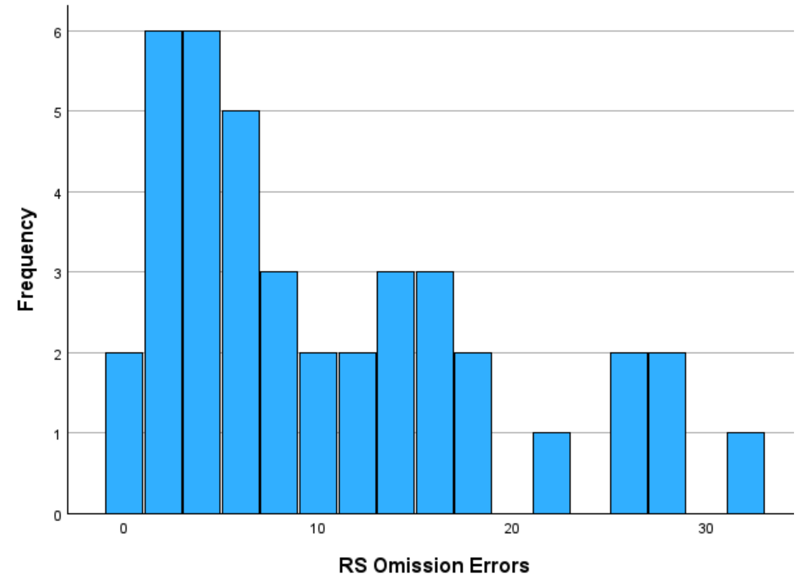


Figure 8

Distribution Pattern of RS Inhibitory Errors (n = 40)

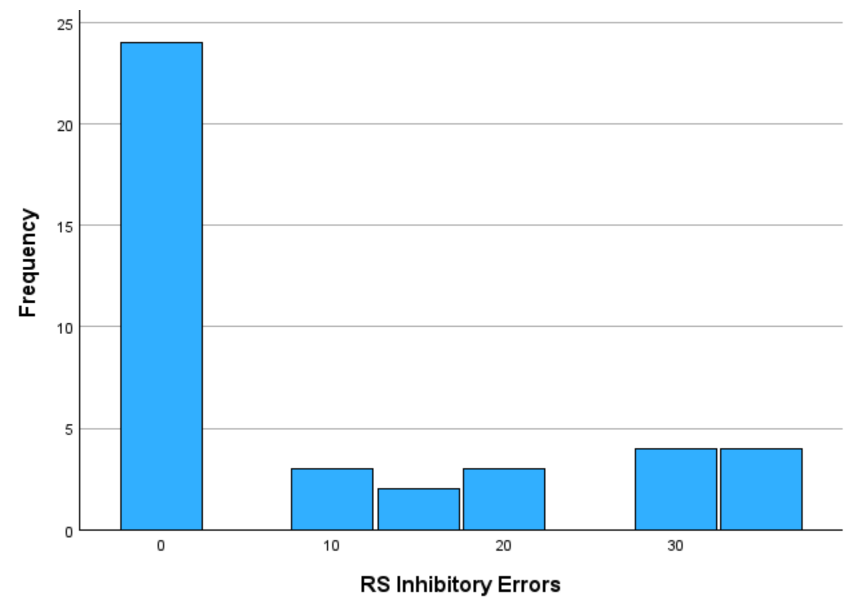


Figure 9

Distribution Pattern of INN Total Errors (n = 40)

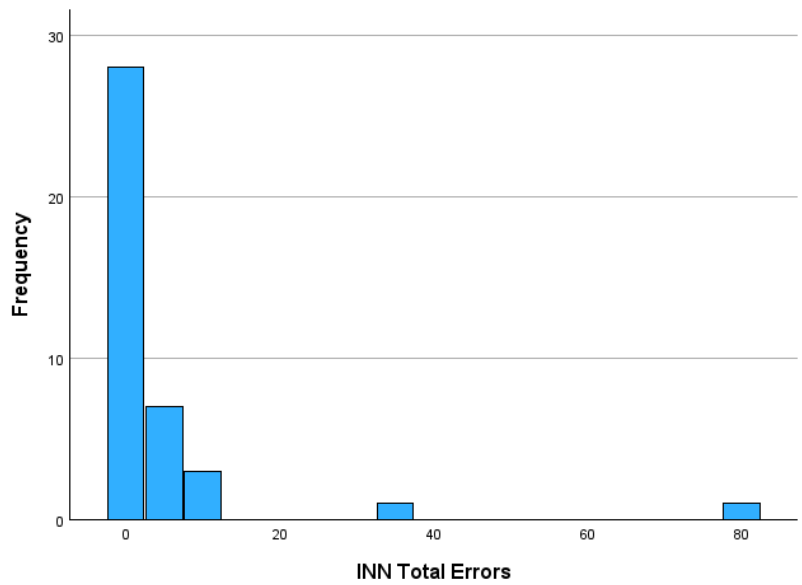


Figure 10

Distribution Pattern of INN Total Completion (n = 40)

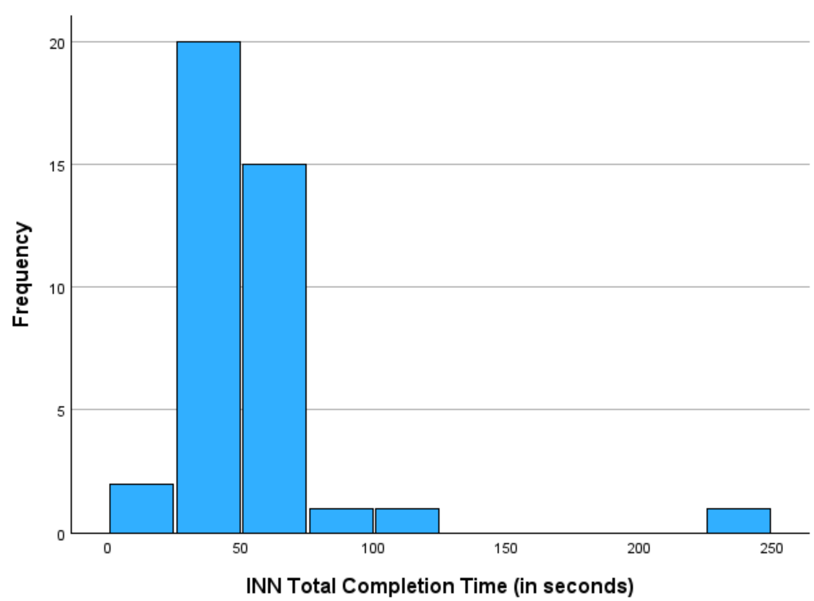


Figure 11

Distribution Pattern of INI Total Errors (n = 40)

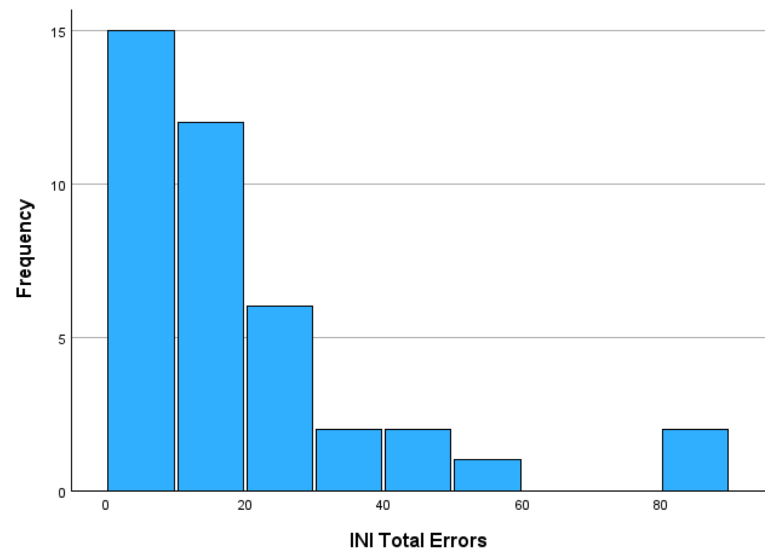


Figure 12

Distribution Pattern of INI Total Completion (n = 40)

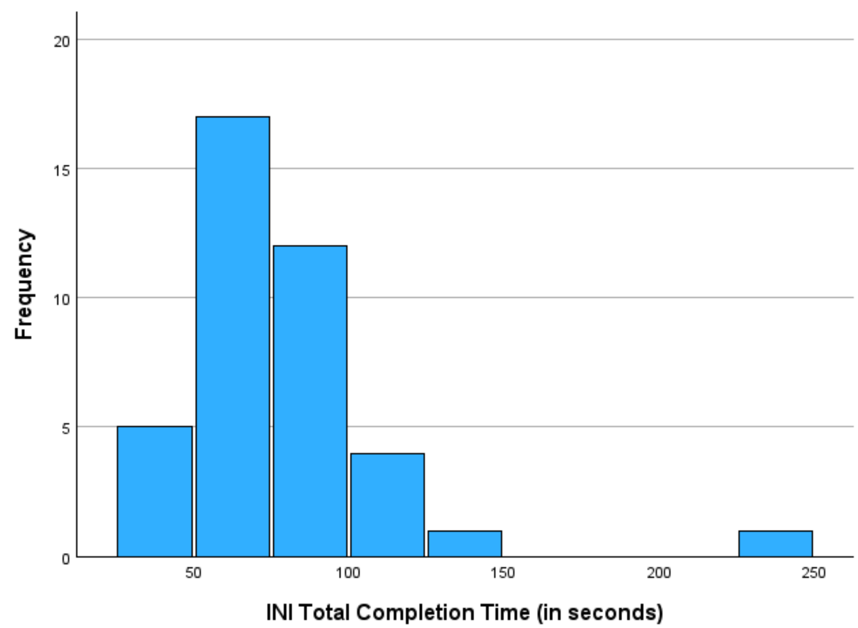


Figure 13

Distribution Pattern of INS Total Errors (n = 40)

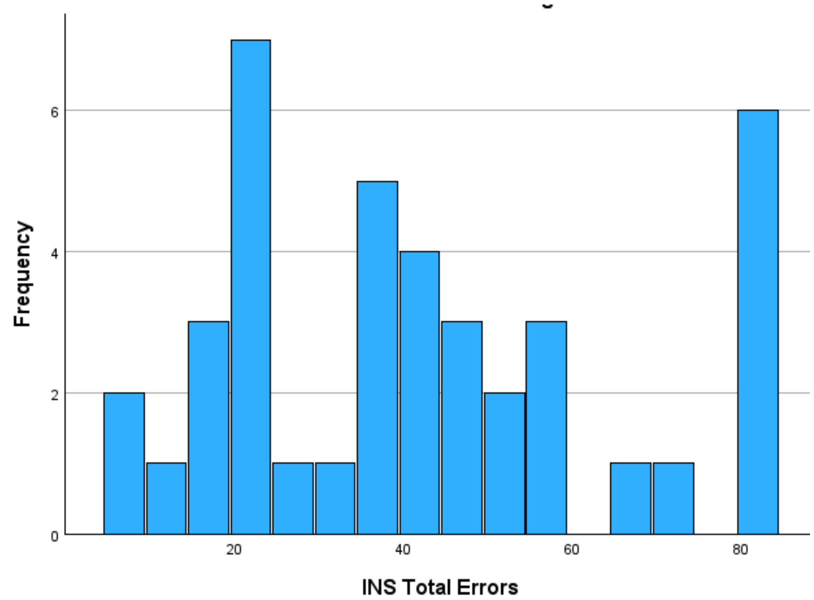


Figure 14

Distribution Pattern of INS Total Completion (n = 40)

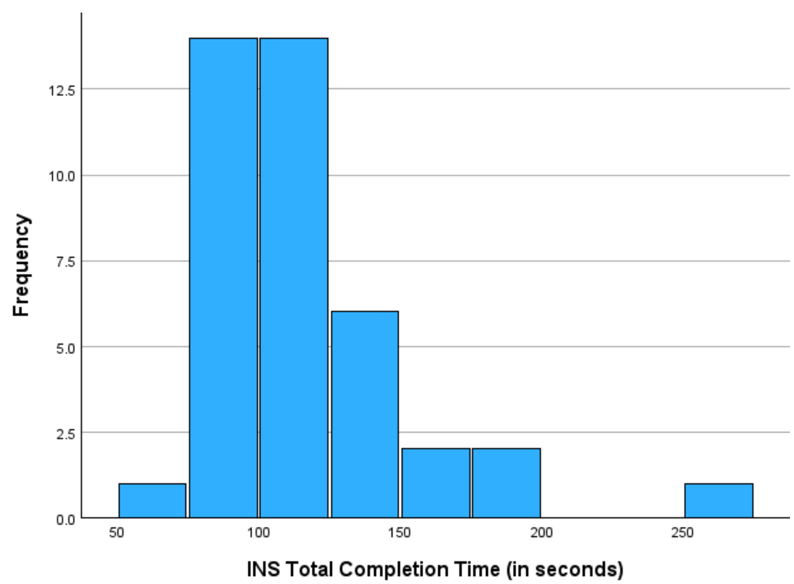


Figure 15

Distribution Pattern of MF Total Score (n = 40)

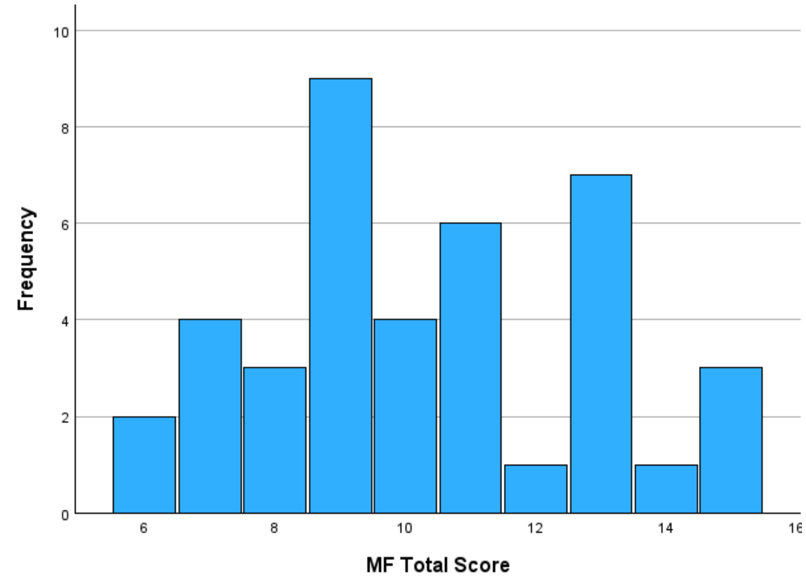


Figure 16

Distribution Pattern of MFD Total Score (n =40)

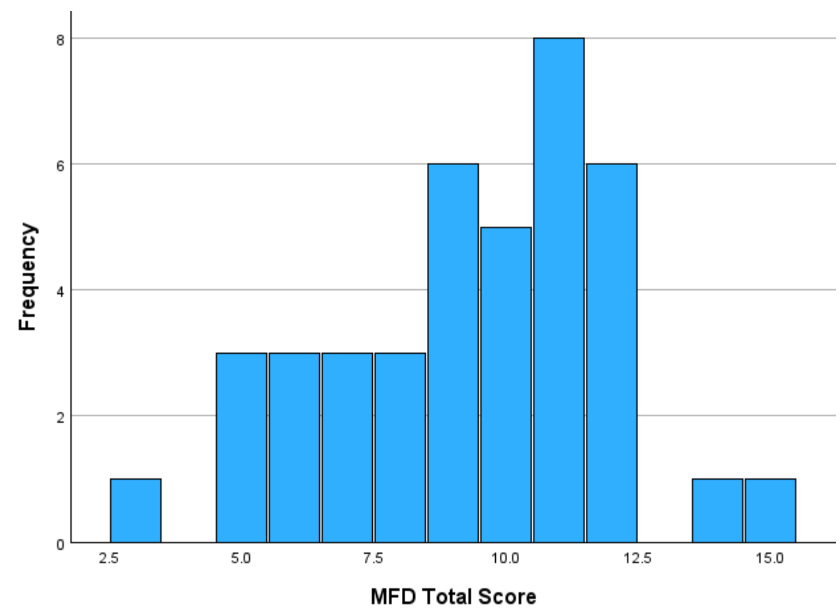


Figure 17

Distribution Pattern of WI Repetition (n = 40)

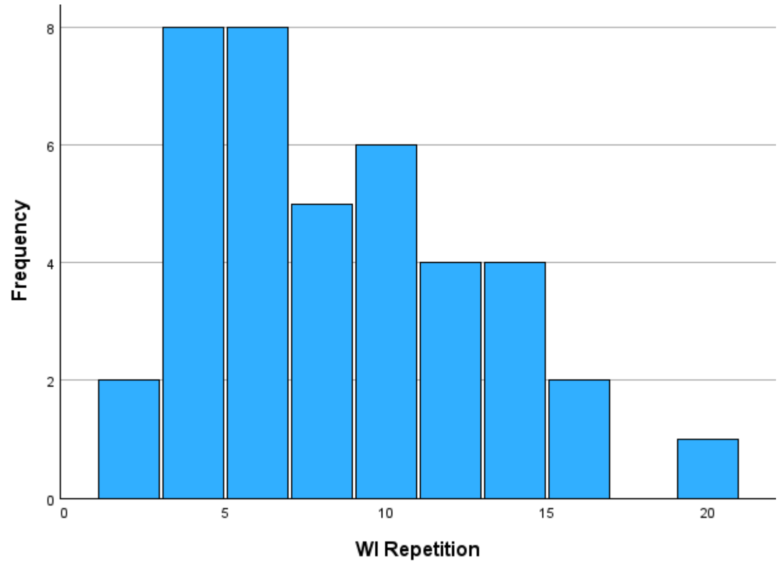


Figure 18

Distribution Pattern of WI Recall (n = 40)

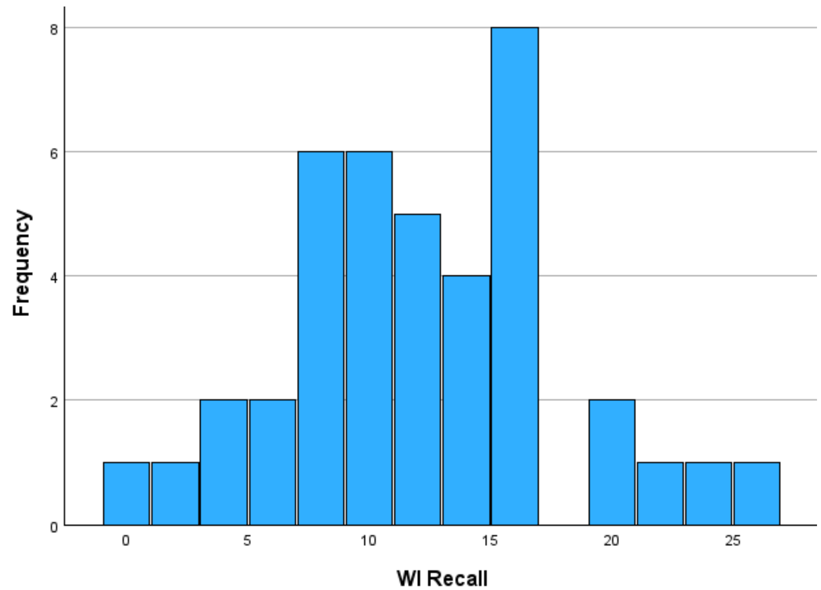


Figure 19

Distribution Pattern of SN Completion Time (n = 40)

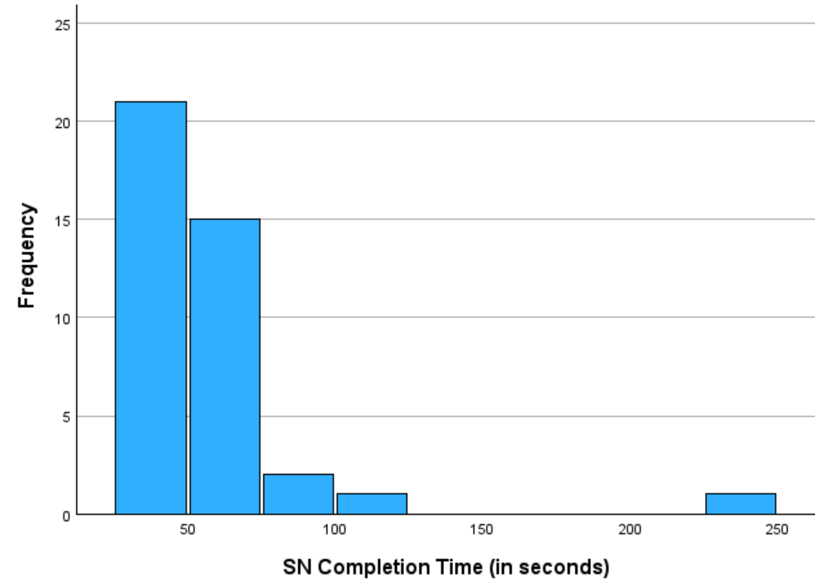


Figure 20

Distribution Pattern of SN Total Correct (n = 40)

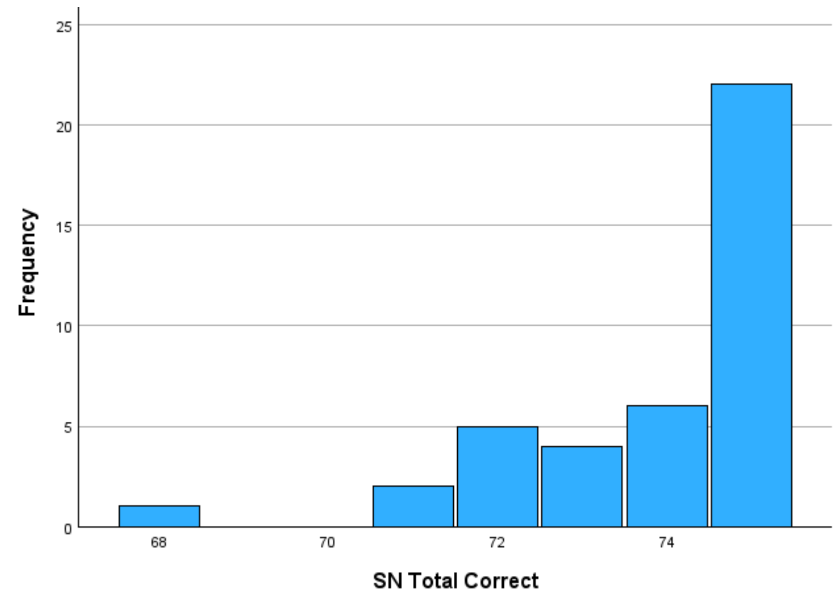


Figure 21

Distribution Pattern of SN Total Self-Corrected (n=40)

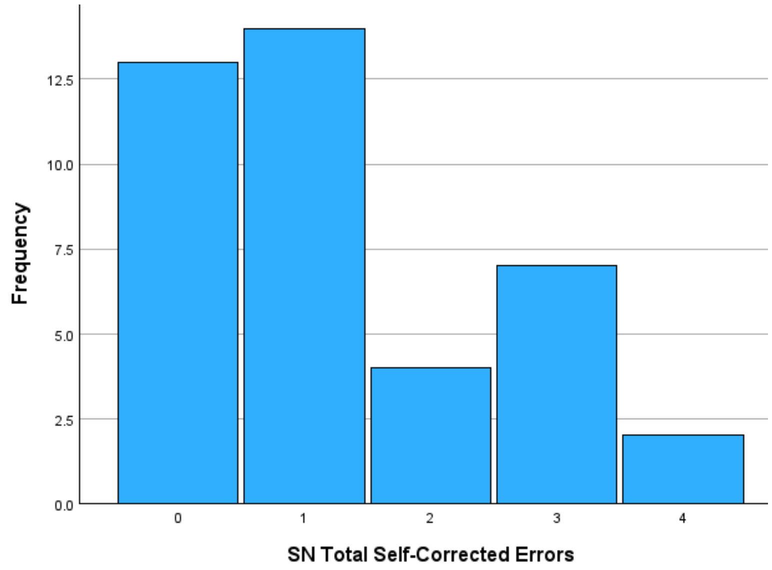


Figure 22

Distribution Pattern of BRIEF Inhibit (n=36)

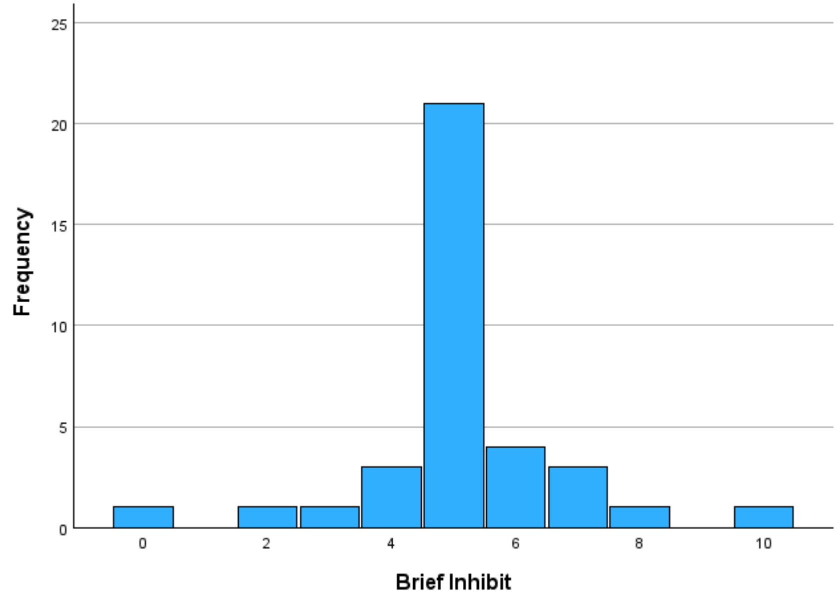


Figure 23

Distribution Pattern of BRIEF Shift (n=36)

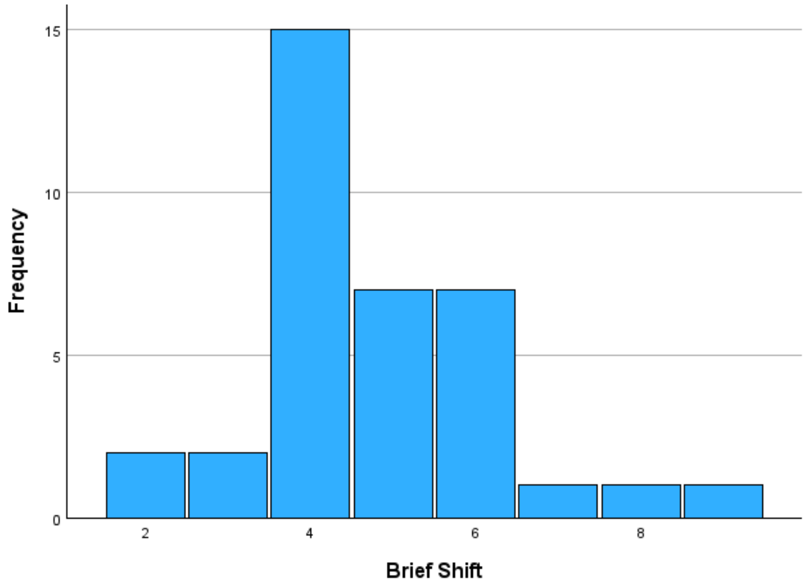


Figure 24

Distribution Pattern of BRIEF Working Memory (n=36)

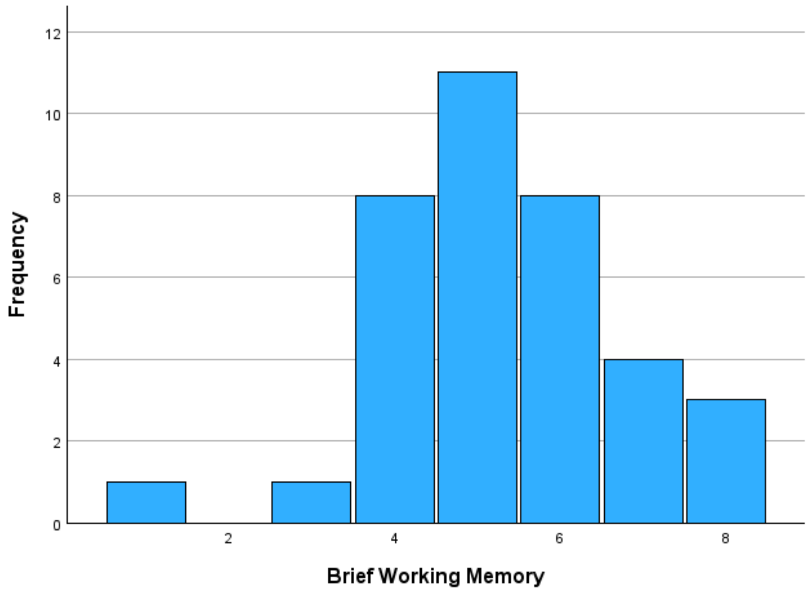


Figure 25

Distribution Pattern of Behavioural Regulation Index (n=36)

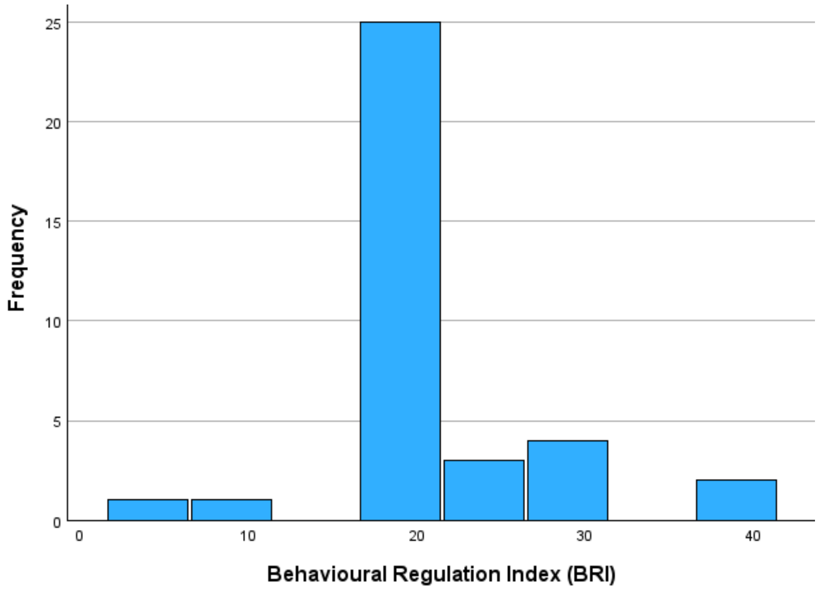


Figure 26

Distribution Pattern of Metacognition Index (n=36)

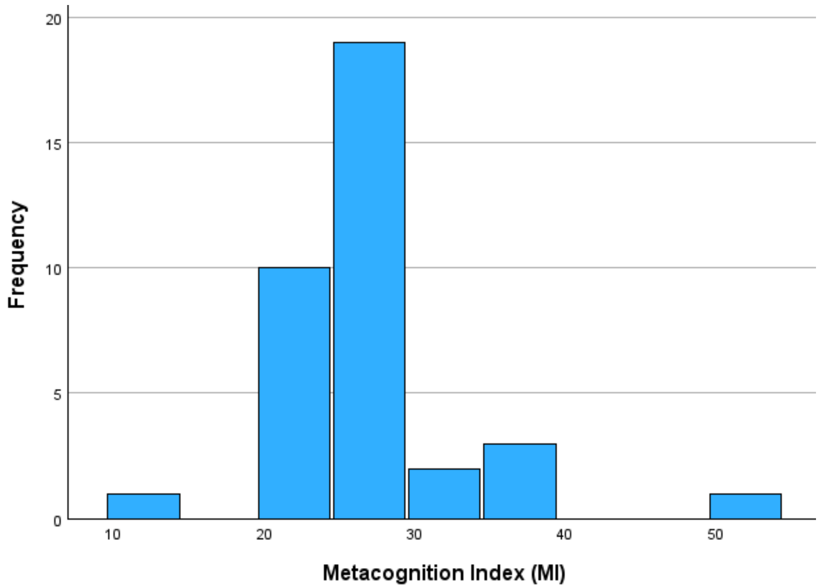
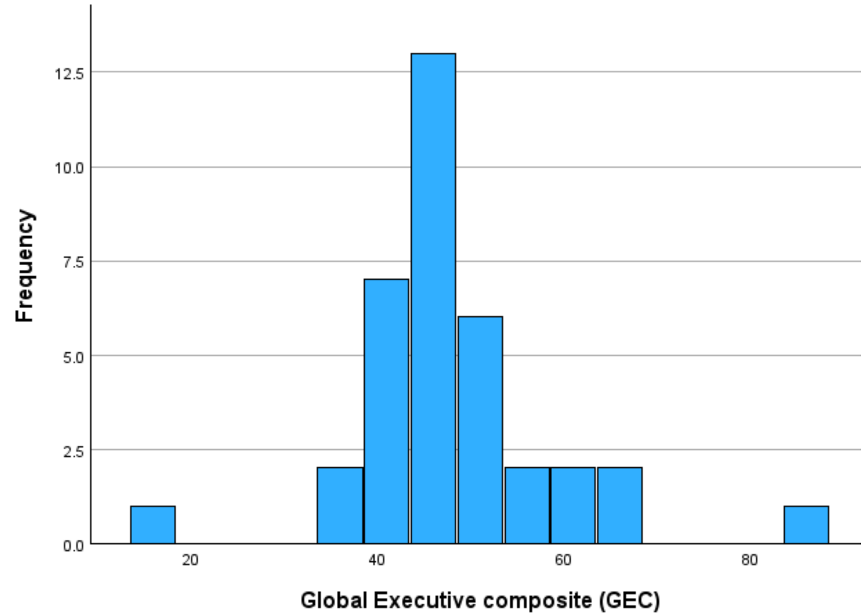


Figure 27

Distribution Pattern of Global Executive Composite (n=36)



Appendix K

Descriptive Statistics

Table K 1

Descriptive Statistics for HIV+ Group NEPSY-II Percentile Rank, Standardised Scores

		Frequencies						
Variable	n	<2	2-5	6-10	11-25	26-50	51-75	>75
Inhibition-Naming INN Total Errors	40	13	1	0	9	0	16	1
Inhibition-Inhibition INI Total Errors	40	27	5	1	3	1	1	2
Speeded Naming SN Total Correct	40	4	6	6	1	1	22	0
SN Total Self-Correct	40	9	2	14	2	0	13	0
Auditory Attention AA Total Correct	35	22	1	1	0	0	11	0
AA Commission Errors	40	30	0	1	0	9	0	0
AA Omission Errors	40	26	2	0	1	1	10	0
AA Inhibitory Errors	40	32	0	0	0	8	0	0
Response Set RS Total Correct	35	18	0	2	5	8	1	1
RS Commission Errors	40	13	0	0	2	1	1	23
RS Omission Errors	40	18	3	5	2	10	0	2
RS Inhibitory Errors	40	16	0	0	0	0	0	24
Inhibition-Switching INS Total Errors	40	37	1	0	2	0	0	0

Appendix L

Table L I

NEPSY-II raw scores for South African Afrikaans-, Pedi-, Southern Sotho-, Tswana-, Xhosa- and Zulu-speaking children (combined), aged 9-11 in Grades 4-6, with disadvantaged quality of education.(Shuttleworth-Edwards & Truter, 2023)

NEPSY-II Subtest	Variable	n	Mean	*SD*
Inhibition-Naming	INN Total Errors	12	2.00	1.81
	INN Total Completion Time	15	56.73	10.17
Inhibition-Inhibition	INI Total Errors	12	5.25	3.74
	INI Total Completion Time	15	70.47	15.49
Speeded Naming	SN Completion Time	17	61.47	17.30
	SN Total Correct	17	73.24	1.48
	SN Total Self-Corrected Errors	17	0.65	1.06
Word List Interference	WI Repetition	18	15.22	3.21
	WI Recall	18	14.83	6.05
Auditory Attention	AA Total Correct	16	27.19	3.49
	AA Commission Errors	16	1.75	3.04
	AA Omission Errors	16	2.63	3.30
	AA Inhibitory Errors	16	0.69	1.30
Memory for Faces	MF Total Score	`15	11.40	1.99
Memory for Faces Delayed	MFD Total Score	15	11.07	3.06
Response Set	RS Total Correct	16	31.13	3.10
	RS Commission Errors	16	1.75	1.73
	RS Omission Errors	16	4.36	3.24
	RS Inhibitory Errors	16	1.69	1.62

Inhibition-Switching	INS Total Errors	11	9.36	5.82
	INS Total Completion Time	15	107.20	21.95

Table L 2

NEPSY-II raw scores for South African Afrikaans-, Pedi-, Southern Sotho-, Tswana-, Xhosa- and Zulu-speaking children (combined), aged 14-16 years in Grades 8-10, with disadvantaged quality of education (Shuttleworth-Edwards & Truter, 2023)

NEPSY-II Subtest	Variable	n	Mean	*SD*
Inhibition-Naming	INN Total Errors	20	1.80	2.14
	INN Total Completion Time	20	48.10	12.13
Inhibition-Inhibition	INI Total Errors	20	3.85	4.39
	INI Total Completion Time	20	60.25	12.24
Speeded Naming	SN Completion Time	20	44.18	12.87
	SN Total Correct	20	74.00	1.69
	SN Total Self-Corrected Errors	20	0.70	0.98
Word List Interference	WI Repetition	12	14.00	3.57
	WI Recall	12	17.92	4.40
Auditory Attention	AA Total Correct	17	28.47	2.18
	AA Commission Errors	17	0.35	0.61
	AA Omission Errors	17	1.35	2.09
	AA Inhibitory Errors	17	0.41	0.71
Memory for Faces	MF Total Score	22	12.73	2.69
Memory for Faces Delayed	MFD Total Score	22	12.86	2.80
Response Set	RS Total Correct	17	33.53	3.18

	RS Commission Errors	17	2.00	4.99
	RS Omission Errors	17	2.00	3.02
	RS Inhibitory Errors	17	0.65	0.86
Inhibition-Switching	INS Total Errors	20	7.55	4.72
	INS Total Completion Time	20	96.59	29.91

Appendix M:

Phase, Duration and Procedure of Mr Zondo's Overarching Study

	Procedure	**Months**	**Instrument**
Phase 1:	Baseline assessment of sustained attention for Experimental **and** Waiting List Control Biosensing of Experimental group	1	NEPSY CPT fNIRS
Phase 2: Experimental group	Intervention	2-6	CPAT Cognitive rehabilitation
Phase 3: Experimental group (2 SDs from Mean Group)	Post testing Assessment & Biosensing	6-8	NEPSY CPT fNIRS
Phase 4	Qualitative Interviews	8-9	
Phase 5: Waiting list control group	Intervention	10-11	
6 MONTHS AFTER PROJECT IS COMPLETE: ASSESSMENT ON INTERVENTION GROUP (Group 2SD from Mean) on NEPSY/CPT			