Investigating the Relationship Between Adverse Childhood Experiences (ACE) and Attention Skills in Children Living with HIV

A thesis submitted in fulfillment of the requirements for the degree of

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by

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Supervised by Mr. Sizwe Zondo

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ABSTRACT

Background: While persons living with HIV (PWH) have benefited from significant advances in antiretroviral (ARV) treatment, neurocognitive deficits sequent HIV, remain elevated in this population. Notwithstanding HIV, adverse childhood experiences (ACEs) have been implicated in compromised neurocognitive outcomes in children living with HIV. There however, continues to be a dearth of research, investigating the intertwined nature of HIV, ACEs, and neurocognition in pediatric and adolescent HIV.

Objectives: This study investigated the relationship between ACEs (High vs Low) and attention outcomes, in children and adolescents, living with HIV, a residing at HIV care shelters in South Africa.

Methods: A non-experimental quantitative research design, inclusive of 42 participants (n = 22 males; n = 20 females), was employed to answer the research questions pertinent to the study. Measures of neurocognition were assessed using the NEPSY-II. Adverse childhood experiences were assessed using the ACE CYW-Qs. Independent Sample t-test and Hierarchical regression analysis were conducted to answer research goals, using jamovi 2.3.21 statistical software.

Results: The study found that participants who reported a high number of ACEs also performed poorly on attention measures. There were inconclusive findings on the effect of biological sex and age, on attention outcomes.

Conclusion: Higher levels of childhood adversities are associated with poorer outcomes in attention scores among children living with HIV.

Keywords: Adverse Childhood Experiences (ACEs), HIV, Attention and Concentration Functions, Neurocognition

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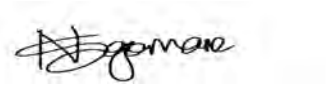
Declaration of Originality

I hereby declare that a quantitative study investigating the impact of adverse childhood experiences on children living with HIV at HIV care shelters in South Africa is my work. All the resources that I have used or cited have been indicated and acknowledged using complete references.



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LIST OF ACRONYMS

AIDS: Acquired Immunodeficiency Syndrome

ANI: Asymptomatic Neurocognitive Impairment

ANT: Attention Network Test

ACEs: Adverse Childhood Experiences

ACE-Q: Adverse Childhood Experience Questionnaire

ARVs: Antiretroviral (drugs)

BBB: Blood Brain Barrier

BCHC: Bayview Child Health Care

CD4+ T cells: Cluster of Differentiation 4 T-helper cells

CNS: Central Nervous System

CSF: Cerebrospinal Fluid

CYW: Centre for Youth Wellness

DC: Dendritic Cells

DNA: Deoxyribonucleic Acid

DTI: Diffusion Tensor Imaging

HAD: HIV-Associated Dementia

HAND: HIV-Associated Neurocognitive Disorders

HIV: Human Immunodeficiency Virus

HIV+: Human Immunodeficiency Virus Positive

HIV-: Human Immunodeficiency Virus Negative

LC: Locus Coeruleus

MMPs: Matrix Metalloproteinases

PPL: Posterior Parietal Lobe

RAS: Reticular activating system

RF: Reticular Formation

RCT: Random Controlled Trial

RNA: Ribonucleic Acid

TBSS: Tract-Based Spatial Statistics

UNAIDS: United Nations Programme on HIV and AIDS

WHO: World Health Organisation

CHAPTER 1: INTRODUCTION

1.1. Context and Rationale

HIV infection during infancy is linked to rapid disease progression. Of relevance to my research, HIV-related Central Nervous System (CNS) dysfunction is associated with neuronal dysfunction, leading to HIV-associated neurocognitive disorders (HAND) (Smith et al., 2008). Significantly, research indicates that children living with HAND are likely to experience developmental delays and significant impairment in multiple cognitive domains, including, but not limited to, learning difficulty, dysexecutive functions, deficits in visuospatial skills, and decreased attention skills Iudicello et al., 2019; Ogishi & Yotsuyanagi, 2018). Importantly, although there has been a decrease in HIV mortality rates since the introduction of highly active antiretroviral (HAART), children continue to experience HAND, namely due to the neurotoxicity of antiretroviral drugs (Boivin et al., 2019; Koekkoek, et al., 2008; Laughton et al., 2018).

As it pertains to this current study, merging research indicates that HAND in children is further compounded by other factors such as poorly resourced environments, lack of cognitive stimulation, and environmental toxins (Anand et al., 2017), and most significantly, for my research, 'adverse childhood experiences' (ACEs) (Young-Wolff et al., 2019). ACEs are defined as traumatic events that occur before the age of 18. ACEs have been indicated to significantly compound HAND (Asmussen et al., 2020) and cause a delay in cognition (Pocuca et al., 2020). The nascent HIV literature consequently indicates that contextual factors such as socioeconomic status and child adversity are intricately linked to HIV neurocognition. A seminal study by (Underwood et al. (2014) found that approximately 50% of South African children from a low socioeconomic (SES) environment, on ARVs indicated cognitive dysfunction despite adhering to strict combination ARVs to reverse HAND.

Similarly, a larger cohort study by Hammond and colleagues (2019) found that South African children from a low SES background, receiving efavirenz (a non-nucleoside reverse transcriptase inhibitor) showed no cognitive gains following a strict ARV regimen. The above findings link to the effect of adverse circumstances as a key covariate in HIV neurocognition (Hammond et al., 2019). Despite the above-established relationship between HIV neurocognition, limitations of HAART, and ACEs, there is a dearth of research investigating the effect of adverse childhood experiences on HIV neurocognition (Santoro et al. (2021).

1.2. Theoretical and conceptual framework

1.2.1. Conceptual Framework

Grant and Osanloo (2014), describe a theoretical framework as one that is based on existing theory relevant to the research topic, and as such, builds on the research inquiry. Further, according to the authors, a theoretical framework has multiple benefits, including providing structure and situating a study within a greater context. With reference to situating my study within a larger theoretical framework, this study draws from several theories and conceptual frameworks, including the biopsychosocial model, stress and developmental psychopathology and Piaget's Cognitive Development Theory. Diverse theoretical lenses allowed for interpreting disparate results, from a vulnerable population, as is the case in this study.

1.2.2. Biopsychosocial model

The model considers the interaction between biological, psychological, and social factors, in shaping health outcomes. In the context of the current study, the model aids in understanding how adverse experiences during childhood, including trauma, stress related to HIV, and illness influence biological processes, psychological development, and social functioning, in the context of attention. To this end, research (e.g., Antinori et al., 2007)

indicates that children and adolescents living with HIV may experience adverse biophysical changes, due to the virus's impact on the central nervous system.

The aforementioned biophysical changes may in turn affect cognitive processes such as attention and emotional processes regulation processes (Antinori et al., 2015) (Concerning genetic vulnerability sequent HIV, genetic factors such as CCR5-Δ32, APOE genotype, HLA alleles, MMP-9 genotype, and SDF-1 variations significantly influence susceptibility to HIV infection and the progression of neurological complications. These genetic markers can affect immune responses, viral replication, and neuroinflammation, highlighting the importance of genetic research in understanding HIV's impact on the CNS (McLaren & Fellay, 2021).

Variations in certain genes can affect a person's vulnerability to HIV infection and the effects it has on the central nervous system. One mutation that can offer resistance to HIV infection or halt its spread is the CCR5-Δ32 mutation in the CCR5 gene, which results in a nonfunctional receptor. This mutation modifies HIV's capacity to enter cells, which impacts the amount of viral load and possible involvement of the central nervous system (Meyer et al., 2022). Once HIV infection is established, genetic factors can modulate the severity of CNS complications.

Variants in genes such as APOE can impact the progression of HIV-related neurocognitive disorders. For instance, the APOE ε4 allele has been linked to an increased risk of developing HIV-associated neurocognitive disorders (HAND) due to its role in neuroinflammation and amyloid metabolism (Avci et al., 2018). The biopsychological model, when further considering psychological factors, and adversities (ACEs), such as parental neglect, and / or abuse, links, ACEs, to chronic stress, and dysregulation of the Hypothalamic-pituitary-adrenal (HPA) axis, when has been indicated to affect cognitive processes, such as attentional control (Teicher et al., 2016).

1.2.3. Stress and Coping Theory

The Stress and Coping Theory examines how individuals perceive and respond to stressors in their lives and how they use numerous strategies to manage stress and its effects (Micha, 2017). The theory makes emphasises the dynamic interaction between people and their environment in the context of stress (Banerjee et al., 2022). With reference to HIV, the theory posits that children living with HIV, may confront many stressors, including health-related, stigma, and disrupted family dynamics, and these stressors can contribute to increased levels of chronic stress, which adversely affects their neurocognitive development and overall well-being (Banerjee et al., 2021; Huang et al., 2020).

The theory further postulates that stressors, such as as chronic health problems, stigma, and family disruptions, often outweigh one's coping efforts, such as seeking social support or engaging in problem-solving strategies, leading to affective disturbances leading to anxiety and undesirable distressing symptoms, which may exacerbate cognitive impairments and impact overall psychological well-being (McManus et al., 2022;Palamarchuk and Vaillancourt, 2021).Related to HIV, the theory posits that adversities such as HIV, may result in avoidant coping mechanisms (Banerjee et al., 2022)). As such, children living with adversity, such as HIV, may undertake coping mechanisms that could influence their cognitive abilities, such as their ability to adapt academically and socially (Li et al., 2017).

1.2.4. Developmental Psychopathology Perspective

According to Hawes and Allen, 2023, developmental psychopathology, broadly defined as the scientific study, to integrate psychopathology and developmental science, with an aim to describe the emergence of psychopathological development, is critical to understand, the cause of mental illnesses in childhood. The theory/rationale of the cojoined perspective of psychopathology, and development, emphasises that risks and protective factors shape the developmental path. To this end, studies (e.g., Shonkoff et al., 2012; Zanolie et al., 2022)

applying the developmental psychopathology, lenses, indicate that ACEs such as trauma or neglect, may disrupt childhood development and increase the risk of children developing cognitive difficulties, particularly in the context of chronic health, in cases such as HIV (Hemelaar et al., 2019)

To this end, Rakesh and Whittle, 2021, contend that positive parenting, for example, may mitigate the impact of developmental psychopathology, on cognition. . For example, a RCT by Valadez et al. (2020), investigated the impact of early parenting intervention (Attachment and Behavioural Catch-Up: ABC) on children's neural processing and psychosocial functioning. Participants (n = 68, Mean Age = 10.0 years) comprised of a comparative group of low-risk children ([1]n = 22) and high-risk children [2](n= 46), whose parents were randomised assigned to receive the ABC (n = 22), or to the control group (n = 24).

Findings from functional magnetic resonance imaging (fMIR), indicated that children who received the ABC intervention demonstrated more differentiated neural responses to their mother's face compared to the control group. Specifically, the ABC intervention group exhibited enhanced neural processing related to attachment and emotional regulation, reflecting improved psychosocial functioning and sensitivity to parental cues (Valadez et al., 2020).

In conclusion, this demonstrates that early parenting interventions, such as the Attachment and Behavioural Catch-Up (ABC) program, can significantly enhance children's neural processing of parent cues and improve psychosocial functioning. Furthermore, this

[1] These are typically children who come from stable and supportive family environments with minimal exposure to factors that could negatively impact their development. In the context of this study, low-risk children are those who do not exhibit significant signs of early-life adversity or dysfunction and whose parents are generally perceived as providing adequate emotional and behavioural support (Valadez et al., 2020).

[2] These children are at increased risk of developmental challenges due to adverse conditions such as exposure to trauma, neglect, or other forms of early-life stress. High-risk children often come from environments characterized by instability, which can impact their emotional and cognitive development. In this study, high-risk children are those whose parents were likely facing more significant challenges or stressors, which might affect their parenting and, consequently, the child's development (Valadez et al., 2020).

suggests that early, targeted interventions can positively influence the developmental trajectories of children, particularly those at higher risk, by enhancing attachment-related neural mechanisms and overall emotional regulation.

1.2.5. Social Cognitive Theory

In relation to the above theoretical paradigms, the study also considered the social cognitive theory. The theory postulates that individuals learn by observing others and that exposure to adversity may serve as models for maladaptive patterns (Bandura, 1986).Similarly, the theory posits that social support, and effective coping strategies, play an important role in managing stress, adversity and learning cognition (Bandura, 1986).The theoretical lens, thus provides, an understanding of the effects of social context, in mitigating adversity, and context, such as learning and cognition, and helps explain positive outcomes in cognitive performance, in children living with HIV, who may receive adequate social support, and coping strategies, in the context of improved cognitive outcomes, despite adversity (Bandura, 1986).

1.2.6. Piaget's Cognitive Development Theory

Piaget's Cognitive Development Theory served as a foundation for explaining qualitative changes in cognitive processes, occurring through the interaction of children with their environment (Piaget, 1971). Piaget's Cognitive Development Theory states that cognitive development occurs through four distinct stages: sensorimotor (0-2 years), preoperational (2-7 years), concrete operational (7-11 years), and formal operational (12 years and up) (Piaget, 1971). This study made use of these four cognitive development stages to examine how Adverse Childhood Experiences (ACEs) may affect cognitive development in children. Research indicates that ACEs can impact cognitive development differently across these stages in the vulnerable population (Huang, 2021). For instance, during the sensorimotor stage, ACEs such as neglect can severely hinder the development of basic sensory and motor skills. In the

preoperational stage, trauma and stress can affect language acquisition and symbolic thinking (Hambrick et al., 2019). During the concrete operational stage, ACEs may disrupt logical reasoning and problem-solving abilities. In the formal operational stage, exposure to chronic stress and trauma can impair abstract thinking and higher-order cognitive processes (Shi and Qu, 2021).

Piaget's Cognitive Development Theory states that cognitive development is based on sensorimotor, preoperational, concrete operational, and formal operational (Piaget, 1971). In relation to the environment, and how ACEs affect cognitive development, research indicates that ACEs can severely disrupt cognitive development by altering the child's environment in ways that impede healthy brain growth and functioning. Adverse environments associated with ACEs, such as exposure to chronic stress, neglect, and trauma, can lead to significant alterations in brain structure and function.

These changes often result in impaired cognitive abilities, including deficits in attention, memory, and executive function. Specifically, chronic stress from ACEs can affect the hippocampus and prefrontal cortex—regions critical for learning and cognitive control—leading to long-term developmental and cognitive challenges (Shonkoff et al., 2012).Additionally, environments marked by ACEs often lack the supportive and enriching interactions necessary for optimal cognitive development, further exacerbating cognitive impairments (Gladieux et al., 2023; Chi et al., 2022).

1.3. Statement of the Problem and Research Objectives

Once HIV enters the central nervous system, it affects cognition leading to HAND. To date, ARVs do not reverse HAND, meaning children continue to experience cognitive deficits besides being on a course of ARVs (Yuan & Kaul, 2021). A review of the literature indicates that, to date, there is only one published study in Sub-Saharan Africa (Santoro et al. 2021) investigating the effect of adverse childhood adversity on HIV neurocognition.

In their study, Santoro et al. (2021) found that high levels of childhood adversity were a significant predictor of poor cognitive outcomes, in key cognitive domains related to HAND. The limitation of the Santoro et al study is that, although the first to investigate the relationship between HAND and ACEs, the study employed an ACE questionnaire designed to study ACEs amongst individuals 18 years or older, although participants in the study were South African adolescents between the ages of 14 -17 years of age. It suffices that the use of an inappropriate scale might have influenced the validity and reliability of the study, and subsequent findings on the outcome variables used in the study (NEPSY-II). Secondly, Santoro et al. (2021) did not determine which ACEs were most prevalent and which could have likely affected neurocognition. Based on the above-identified limitations, Santoro et al. (2021) recommended further research be undertaken to investigate the intertwined nature of the relationship between ACEs and HIV neurocognition.

1.4. Response to Statement of the Problem

The study developed on the preliminary findings of Santoro et al. (2021), by investigating the relationship between ACEs and HAND in a nonclinical sample of children living with HIV. Children were based in two shelters caring for children living with HIV located in Johannesburg, South Africa. The deviation from the Santoro et al. study is that this particular study focused on children living with HIV aged between 10-16 years. Additionally, as recommended by Santoro et al. (2021), the study employed validated neuropsychological measures, namely the NEPSY-II and appropriate age-related ACEs measures. As opposed to Santoro et al. (2021), who investigated working memory and executive functions, this study investigated the effect of ACEs on sustained attention and executive functions using the NEPSY.

Moreover, when considering the vulnerabilities of children living with HIV, the effects of ACEs may be significantly magnified, especially for those living in HIV care settings. Due

to the limited research on the impact of ACEs on cognition, in particularly in children living in HIV care shelters, the study, in addition to the above, sought to understand the interaction, between ACEs, cognition, and HIV, among children living in care shelters. To this end, , it was important to focus on children living with HIV in shelters, due to multiple factors, including, but not limited to (a) dual vulnerabilities – defined as the combined impact of chronic health conditions and exposure to adverse environmental conditions, which can compound the risks of cognitive and developmental impairments (Hughes et al., 2017).

Secondly, due to (b) unique contextual circumstances, such as the instability and high-stress environments typical of care shelters: children living in care shelters with HIV frequently encounter specific contextual circumstances, such as frequent relocations, disrupted familial and social relationships, and limited access to consistent medical and psychological care. These factors can exacerbate the cognitive effects of Adverse Childhood Experiences (ACEs) by creating an environment that amplifies stress and disrupts developmental processes critical for cognitive and emotional growth (Evans et al., 2013; Shonkoff et al., 2012).

Most children living in care shelters frequently encounter specific contextual circumstances, such as high levels of instability due to frequent relocations, inconsistent caregiving, and exposure to traumatic experiences. These circumstances include frequent changes in caregivers and environments, limited access to stable and supportive relationships, and exposure to environments characterized by neglect or abuse. Such factors can contribute to elevated stress levels and disrupt normal developmental processes, exacerbating the cognitive and emotional effects of Adverse Childhood Experiences(ACEs) (Manyema & Richter, 2019). Additionally, the lack of a stable and nurturing environment can hinder the development of secure attachments and coping skills, further impacting cognitive and emotional outcomes that can exacerbate the cognitive effects of (ACEs) (Dykes, 2016). Kang et al. (2016), further state that, the frequent changes in care home, and having limited access to

services and resources, such as mental health support and educational assistance, are some examples of these factors. These conditions may result in heightened stress and instability, which can negatively impact cognitive and emotional development in children living in care shelters. Such disruptions and inadequacies in support services can exacerbate the effects of Adverse Childhood Experiences (ACEs), leading to increased risks of developmental delays, behavioural problems, and difficulties in emotional regulation (Godoy et al., 2018; Doewes et al., 2021).

Given the above, the research aimed to investigate the impact of ACEs on children living with HIV in a South African setting. As indicated above, studies suggest that adverse childhood experiences may be associated with attentional difficulties in children living with HIV, than in the general population (Pocuca et al., 2020). Notwithstanding, there is a dearth of studies investigating adverse childhood experiences, and their effect on attention processes, amongst children living with HIV, and placed in HIV care shelters. Summarily, the research study investigated the degree of ACEs experienced (High vs Low), and how ACE severity, is associated with attention deficits, in a sample of children living with HIV, residing in HIV shelters in South Africa.

1.5. Research Methods, Procedures, and Techniques

This research gathered and investigated data on attention (sustained and executive attention) and the effect of ACEs on attention skills, in children living with HIV, using a quantitative approach. The quantitative approach is described as a process that uses numerical data, to analyse and extrapolate the data to a larger population (Chan et al., 2019). Since no experimentation was undertaken, the study took the form of a descriptive, and non-experimental design.

Data collection for the project was conducted between July 2022 and November 2022. Purposive sampling was used to recruit 42 research participants. Participants were assessed by Mrs Sibongile Ngomane, a student researcher, and also a registered Independent Psychometrist (PMT 0099694). All data was collected independently, in a quiet room, equipped with a chair and table. Each participant was assessed for about one and a half hours in total. Dependent measures for adversity included the Child Adversity Experiences Questionnaire (Adverse Childhood Experiences Questionnaire: CYW ACE-Q *Teen*); and the Adverse Childhood Experiences Questionnaire (CYW ACE-Q *Child*). Neuropsychological data was obtained using the NEPSY-II assessment.

1.6. Thesis Structure

The context, justification, and significance of the study are all presented in the current chapter (Chapter 1). Chapter 2 reviews relevant literature on HIV, neurocognition and ACEs. Chapter 3 details the research design, methods, data collection techniques, and ethical considerations pertinent to my research study. Chapter 4 presents results pertaining to the study. Chapter 5 discusses the findings of the research in light of the HIV and ACEs literature. The chapter concludes by providing limitations and suggestions for future research.

1.7. Summary of Findings

Key findings from the study indicate that participants experienced at least one adverse childhood experience (ACEs). For the most part, the study found that the prevalence of ACEs was high amongst children in the study. Pertinent to these findings, participants exposed to a higher number of ACEs, indicated poorer attention and concentration outcomes, compared to those with fewer reported ACEs. For the most part, females performed better than males on attention and executive functions. When comparing participants' outcome measures on

attention, participants in primary school performed better than those in high school on attention measures.

CHAPTER 2: LITERATURE REVIEW

2.1. HIV Epidemiology

The Human Immunodeficiency Virus (HIV) poses a serious threat to public health. Recent data indicates that approximately 85.6 million individuals have been living with HIV since its discovery (UNAIDS, 2023). Of those infected, 20.8 million people were living in Eastern and Southern Africa. Approximately, 4.8 million reside in Central and Western Africa and 6.5 million (15%) in Asia and the Pacific (UNAIDS, 2023). Further epidemiological data indicates that South Africa has the highest rates of people living with HIV/AIDS (PLWH), amounting to approximately, 7.8 million (UNAIDS, 2023). Of relevance for my research, epidemiological data indicates that there are approximately 520 000 adolescents and children aged 10-19 years (Children and AIDS, 2021) living with HIV, and 230 000 of these children are in South Africa.

2.2. The Neurobiology of HIV/AIDS

Microbiologically, HIV is a retrovirus that attacks cells in the immune system (Kurapati et al., 2016). Retroviruses have been linked to multiple diseases that affect the neurological and immune system, leading to hemolytic anemias, cancers, and immunodeficiency syndromes (Mavhu et al., 2020). HIV has since been isolated into two distinct strands, namely HIV-1 and HIV-2. The HIV 1 type is the most prevalent and primarily affects active CD4+ lymphocytes, macrophages, monocytes and dendritic cells (Vérollet et al., 2015).

As a retrovirus, HIV uses the enzyme, reverse transcriptase to transform viral RNA into DNA, infecting CD4+ T cells and macrophages (Kurapati et al., 2016). Due to tropism and drug resistance, HIV continues to be a significant health challenge (Kurapati et al., 2016). Of the different clades of HIV (A, B, C, D, F, G, H, I, J, and K), the C subtype clade is the most

dominant subtype found in Southern Africa and India, and continues to be to be most virulent (Milligan & Cockcroft, 2017).

2.3. The Trojan Horse Hypothesis

The "Trojan Horse" hypothesis, states that HIV enters the brain by crossing the Blood Brain Barrier (BBB[3]). Specifically, the hypothesis postulates that through a poorly understood mechanism, infected macrophages and monocytes enter the brain during the early course of HIV infection (Hult et al., 2008; Kurapati et al., 2016). In vitro HIV studies indicate that the BBB becomes more permeable when HIV infects astrocytes, leading to nerve cell necrosis and aberrant neural transmission, resulting in neurocognitive challenges observed in HIV infection (Eugenin et al., 2011). Importantly, evidence suggests that infected astrocytes and macrophages are reservoirs for the proliferation of HIV once the virus crosses the BBB, leading to structural changes in the cerebral cortex (Boivin et al., 2019).

Further to the above, once in the cortex (brain), HIV decoupling in the form of viral glycoproteins (gp120, p17, p24), is thought to infect nerve cells and impair neurotransmission, leading to neurological damage (Kuhn et al., 2017). Regarding neural transmission, HIV impairs catecholamines, a class of neurotransmitters including dopamine, norepinephrine, and epinephrine (adrenaline) (Rovnaghi & Anand, 2018). Catecholamines are indicated for neurocognition and are implicated in attention, working memory, and executive functions, and their dysregulation, is associated with disturbed nerve cell signalling, further contributing to neurological and cognitive deficits observed in neuro HIV (Rovnaghi & Anand, 2018).

2.4. Cortical Regions Implicated in HIV: The Fronto-Striatal Network

Linked to the above, HIV has been demonstrated to disturb the architecture of the cerebral cortex. Ogura et al. (2017) investigated the relationship between HIV infection and

[3] The Blood Brain Barrier (BBB) is composed of sspecialized microvascular endothelial cells interacting with astrocytes (Hult et al., 2008).

changes in frontostriatal intrinsic connectivity within the cortex. Findings indicated that when compared to controls, PLWH indicated attenuated connectivity within the frontostriatal network as measured by functional magnetic resonance imaging of the cortex (Ogura et al., 2017). Neural circuit disruptions are not unique to the frontostriatal network; research has indicated that deep white matter structures connected to the frontostriatal, and thalamic neural circuitry (Chan et al., 2019; Zayyad &Spudich, 2015) are aberrant due to HIV infection. A key consideration from the above is that dysregulations of the frontostriatal network is implicated in deficits linked to executive functions and attention (Kuhn et al., 2017), and processing speed (Zayyad & Spudich, 2015).

2.5. ARVs and HIV

ARVs have been vital in curtailing HIV developing into AIDS. Before the dawn of ARVs,, population-based HIV-AIDS prevalence surveys in Southern Africa consistently indicated HIV prevalence rates of 8 - 12% among adolescents (Laughton et al., 2018). However, there has been a decline in the prevalence of HIV among young children due to the increased intake of ARVs (Yuan & Kaul, 2021). Moreover, with decreased prevalence rate, the life expectancy of children living with HIV, especially in low-middle-income countries, has significantly increased (Chaudhury et al., 2017) Despite the above improvements, the prevalence of HIV Associated Neurocognitive Decline (HAND) in the era of ARVs remains high (Nastri et al., 2023). Although not clearly understood, antiretroviral medications have been implicated to exacerbate HAND, namely due to their neurotoxicity, which has been linked to neuronal dysfunction (Nastri et al., 2023). For example, a study by Nastri et al. (2023) indicated that Didanosine, a nucleoside reverse transcriptase inhibitor (NRTI), has been linked to neurotoxicity, leading to greater levels of HAND.

2.6. HIV-Associated Neurocognitive Disorders (HAND) and Attention

According to the Frascati criteria, besides the use of laboratory and imaging testing, HAND is diagnosed if a patient scores suboptimal on nadir CD4+ T-cell counts and presents suboptimal on neuropsychological performance on at least three cognitive domains, related to either, executive functions, episodic memory, speed of information processing, motor skills, attention /working memory, language, and sensory perception (Zenebe et al., 2022; Yuan and Kaul, 2021). Based on the above HAND diagnosis, the prevalence rates of HAND vary from as low as 7.3% to a high of 85% worldwide (Zenebe et al., 2022). Moreover, according to Iudicello et al. (2019), HAND impairment rates vary by HIV clade, with the C Clade presenting with the greatest levels of HAND prevalence (Iudicello et al., 2019). One study (Joska et al., 2011), estimated the prevalence of HAND to be approximately 76 percent, in a sample of untreated PLWH living in South Africa.

Although HAND causes general cognitive decline, cognitive domains most affected include psychomotor disturbance, information processing speed, executive functioning, working memory, sensory perception, and attention skills (Yuan & Kaul, 2021). The below, section, details the effects of HAND on attention, and describe the neuroscience of attention and cortical networks implicated in HIV.

2.7. The Neuroscience of Attention and HIV Infection

Attention is described as the primary modality for cognition. As such, other cognitive skills such as working memory, abstract reasoning, and executive functions, including problem-solving are premised on attention (Arif et al., 2020;Posada et al., 2012). Importantly, attention and executive functions are essential for children to succeed in learning environments where they are required to focus for extended periods of time (Lipscomb et al., 2021a).

Various models exist to explain the neuroscience of attention, including Broadbent's, (1958) and the Feature Integration Model of attention, proposed by Treisman, (1964). Posner and Petersen's (1990) Attention Network Model continue to be one of the most widely used models to explain attention. According to the model, attention is divided into three networks: the alerting network, the orienting network, and executive network (Posner & Petersen, 1990). The alerting network is involved in maintaining a state of vigilance to sustain attention for a long period of time. The orienting network accounts for the human ability to select certain stimuli, from multiple sensory stimuli, and to ignore irrelevant stimuli. Lastly, the executive network monitors and resolves conflicts in planning and dividing attention (Posner & Posner, 1990). Anatomically, the frontostriatal, and thalamic regions are implicated in the alerting network (Morris et al., 2016). The superior parietal lobes, and the temporal parietal junction are thought to regulate the orienting network of attention (Petersen & Posner, 2012). Lastly, the anterior cingulate and lateral prefrontal cortical regions are thought be essential for regulating the executive network of attention (Petersen & Posner, 2012). Relevant to my thesis, research indicates that the above neural networks are implicated in HIV.

Wang et al. (2017) used the Attentional Network Test (ANT) to test whether HIV patients showed attentional impairment. Compared to HIV controls, HIV+ patients showed less warning cue preparation for detecting expected or alerting signals. Findings from Wang et al. (2017) were in accordance with the neurotransmitter hypothesis, which hypothesizes that alerting attention, modulated by norepinephrine, may be disrupted in HIV infection. Furthermore, Wang et al. (2017) found that HIV+ participants indicated executive attention network deficiencies (e.g., difficulties resolving and competing for attention cues) when compared to HIV- controls. The Attention Network Test (ANT) was used to determine the attention skills. The ANT is a computer-based test that is given one-on-one that examines the

executive attention, orienting, and alerting networks within a single task. A spatial cueing task is included in the exam (Kirby et al., 2015).

Findings from Wang et al. (2017) are similar to those by Schulte, and colleagues (2005), who found that HIV infection, degrades the fronto-parietal network, a key network that governs selective attention, and executive control[4]. Lastly, Wang et al. (2017) indicate that the orienting attention network is further compromised in HIV+ children, as indicated by aberrant cholinergic levels, key neurotransmitter molecules, vital in maintaining attention levels (Wang et al., 2017).

Further to the above, a review of the literature indicates that paediatric HIV is characterized by difficulties in sustained attention. Hoare et al. (2019) administered the WISC-IV to 12 asymptomatic HIV+ children, and 12 seronegative children, between the ages of 8 and 12 years, matched for biological sex. Results indicated that HIV+ children performed worse on the WISC Digit Span Forward, when compared to healthy controls. According to Hoare et al. (2019), findings from the study are indicative of decreased fractional anisotropy, and demyelination of the corpus callosum, and frontal pole, both observed in paediatric HIV (Hoare et al., 2019).

In a different study, Martin et al. (2006) evaluated sustained attention amongst 41 HIV+ children with mild to moderate brain abnormalities as indicated by computer tomography imaging. When compared to neurotypical controls, HIV+ children indicated aberrant neuronal patterns, and performed significantly worse ($p < 0.05$) on WISC-IV measures for sustained attention (Martin et al., 2006). Interestingly, the study found that ARVs, where not a mitigating factors for aberrant neural networks, or cognitive deficits observed within the sample (Martin et al., 2006). Lastly, Arif et al. (2020) investigated attention skills using

[4] HIV patients in the study performed suboptimal of the Trial Making Test (TMT), and Stroop Task, when compared to controls (Schutle et al., 2005).

magnetoencephalography (MEG), paired with neuropsychological data from the Flanker Test. Results indicated that HIV+ participants responded slower than negative control, on trials requiring attentional reorienting. Interestingly, neuronal dysfunctions, namely decreased prefrontal theta activity, and decreased alpha activity in the left parietal and dorsolateral prefrontal cortex, were linked to deficits on the Flanker task (Arif et al., 2020). Other studies (e.g., Pocuca et al. 2020), have reported similar aberrations in attention skills in individuals living with HIV.

2.8. Adverse Childhood Experiences and Cognition

2.8.1. ACEs and Cognition in The General Population

The literature indicates that exposure to ACEs is associated with impaired cognitive development in childhood (Hughes et al., 2017; Hawkins et al., 2020; Kalia et al., 2021). Carlson (2019) maintains that exposure to ACEs leads to profound changes in developmental pathways, that continue throughout adulthood (Carlson, 2019). Moreover, ACEs are associated with negative outcomes in cognition, psychological well-being, behavioural health, and employment opportunities, to name a few.

ACEs are defined as sequences of traumatic events occurring before the age of 18. According to the 2011–12 National Survey of Children's Health (NSCH), 46% of children in the US experienced at least one ACE and a quarter experienced two or more ACEs (Sacks et al., 2014). Other studies have revealed that at least 90% of adults who reported being exposed to an adverse experience in their childhood, also reported being exposed to one or more adversities post childhood (Guinosso et al., 2016). According to the study, behavioural problems and poor physical health outcomes were correlated with cumulative early childhood ACE exposure (Liming & Grube, 2018). In addition to the above, Webster, (2022) argues that early childhood exposure may have implications, for other aspects of life, including cognition,

and behavioural consequences later in life. The implication of ACEs, on cognitive processes is expounded below.

2.8.2. ACEs and Cognition in Children Living in Care Homes

ACEs present a significant challenge to children's cognitive development, particularly those living in care shelters (Barenbaum & Smith, 2016). When compounded with the burden of being infected and living with HIV, according to Bailey et al. (2018), children living with HIV, are further vulnerable to stigma, discrimination, and complex medical needs, that may exacerbate experiences of trauma, and adversity. According to Rice et al. (2019), the cumulative burden of ACEs and HIV, further impacts cognitive functioning. The authors argue that infected children may be prone to further neurodevelopmental delays, and behavioural challenges, which may affect cognition and academic performance.

2.8.3. ACEs on Academic Performances of Children and Adolescents

According to DelGiudice, 2017 academic performance in children and adolescents, is associated with ACEs, which invariably have an effect on working opportunities, future socioeconomic status, and health . To this end, one of the detrimental effects of ACEs is their association with poor academic outcomes(Duke, 2020;York et al., 2023).Recently, studies have found that ACEs have a negative impact on children and adolescents (Duke, 2020; Qu et al., 2024). However, contradictory to the above, other studies on ACEs and academic performance found that there was no correlation between ACEs and poor school performance.

The cumulative effect of ACEs, on academic performance in children and adolescents, has not been determined in previous systematic reviews and meta-analyses (Mersky et al., 2021a);rather, only quantitative associations between childhood violence and victimisation on academic performance. Qu et al. (2024), investigated the relationship between ACEs, and academic performance among children and adolescents and found that higher levels of ACEs

are associated with lower academic performance. The study highlights that children and adolescents who experience multiple ACEs tend to face more significant challenges in school, including lower grades, increased absenteeism, and reduced engagement (Qu et al., 2024). The researchers suggest that addressing ACEs through targeted interventions and support systems could help improve educational outcomes and the overall well-being of affected students.

With reference to HIV, and academic performance, a systematic review y by Zinyemba et al. (2019) explored the mechanisms that influence educational outcomes, in this population. In their study, the authors considered orphaned children living with HIV. Findings demonstrated that variables such as, financial difficulties, missing school, due to caring after siblings, and lack of motivation led to adverse educational outcomes (Zinyemba et al., 2020). Though this study elaborates on the impact of ACEs on the academic performance and educational attainment of children and adolescents with HIV, it does not further expand on the population of children living in HIV care shelters. Notwithstanding, Qu et al. (2024), indicate that children with one or more ACEs, are 1.36 times more likely to repeat a school grade, compared to those who have not experienced ACEs. Conversely, the risk of repeating a grade in the future increased with the cumulative level of ACE.

2.9. Implications of ACEs on Biological and Cognitive Processes

2.9.1. Neurobiological Consequences

Early traumatic events have been indicated to impact subsequent biological, cognitive, and behavioural processes (Ji and Wang, 2018). Firstly, from a biological perspective, ACEs have been found to result in alterations, in the structural integrity of the hippocampus, temporal gyrus, fornix, limbic system, and corpus callosum regions (Herzog and Schmahl, 2018; Vogel et al., 2020). For example, Buimer et al. (2022) investigated the relationship between ACEs and cortical morphology among 8 to 11-year-old children in Japan. Using functional

neuroimaging, the study found aberrant brain morphology as indicated by cortical thinning and reduced cortical surface area in fronto-subcortical networks. Cortical thinning was linked to early stressors such as children experiencing and living with early parental bereavement and divorce. Of relevance to my research, Buimer et al. (2022) found that on average, children who were exposed to two or more ACEs reflected less cortical surface area in the left pars triangularis Broca's area, and prefrontal frontal gyrus. Lower fractional anisotropy (white matter connectivity) was also noted in the hippocampi of children who experienced two or more ACEs (Buimer et al., 2022). These morphological findings are important, as loss in brain matter, especially in regions such as the left pars triangularis, and prefrontal frontal gyrus, affects brain functions such as executive functions and attention (Buimer et al., 2022).

Linked to the above, children who witness domestic violence (DV) have been reported to indicate observable alterations in the peripheral and central nervous system, when compared to controls who do not witness DV. Mueller and Tronick (2019), examined exposure to intimate partner violence during early childhood and found that witnessing intimate partner violence (verbal), had an impact on children's cognitive function and intelligence quotient (IQ) outcomes. In their study, Mueller and Tronick (2019), linked low IQ outcomes to dysregulation of the Hypothalamic Pituitary Adrenal Axis (HPA), a structure integral to emotional and cognitive regulation (Mueller and Tronick, 2019). Linked to the above, Touloumakos and Barrable (2020), indicated that parental neglect and experiencing domestic violence, was similarly linked to heightened allostatic load, which altered neurological, and endocrine, regulation, leading to altered cognitive outcomes.

Also related to the above, Lawson et al. (2017) investigated the volumes of the hippocampi and amygdala, in adults between the ages of 25 and 36 years old, who experienced childhood socioeconomic depravity and child abuse (Lawson et al., 2017). The study found that low socioeconomic status conditions and maltreatment were related to reduced

hippocampi, (Lawson et al., 2017).Similarly, the authors found that greater levels of childhood maltreatment, were significantly correlated with reduced amygdala volume. Alterations in hippocampi and amygdala volume were notably greater in females from low SES, childhoods, than men from the same SES upbringing (Lawson et al., 2017). The above findings are similar to those reported by Xu et al. (2021), who reported aberrant electroencephalography (EEG) coherence in the frontotemporal region, as indicated by increased frequency of temporal lobe epilepsy symptoms, in children from low SES who experienced sexual abuse. Beside the above, other studies (e.g., Lipscomb, et al., 2021), have indicated a link between ACEs and disturbed cortical morphology.

2.10. Cognition and ACEs

Notwithstanding the above, parental separation or divorce, has been linked with reduced cognitive and academic outcomes (Anthony et al., 2014). Nusinovici et al. (2018) investigated the impact of parental separation on preterm children's school performance at age five. Preterm children who experienced parental divorce were compared to a cohort who experienced typical neurodevelopmental and did not experience parental separation (Nusinovici et al., 2018). Findings from the Global School Adaptation Questionnaire (GSA) found that when they turned five years old, children born preterm, and who experienced parental separations, were likelier to experience lower school achievement outcomes than controls (Nusinovici et al., 2018). In a similar US study, Brand et al. (2019),found that parental divorce restricts children's access to quality education, leading to limited intellectual achievement, especially in college.

In another study, Tsavoussis et al. (2014), investigated mental health and neurocognitive outcomes amongst children aged between 11 to 14 years of age in Uganda. All children reported experiencing exposure to home violence. Findings indicated that early experiences of family violence, were linked to reduced cognitive and academic outcomes at

primary school (Tsavoussis et al., 2014). Similarly Heleniak and McLaughlin (2020), investigated the effect of exposure to interpersonal violence on cognition and theory of mind (ToM). Findings indicated that teens (ages 8 to 16 years) who experienced interpersonal violence in a community setting, were also likely to experience decreased theory of mind (aggressive behaviour) and less accuracy during cognitive tasks for inhibitory control (Heleniak & McLaughlin, 2020).

This was measured using a Go/No–Go assessment. The researchers also found that poor ToM, was linked to greater externalising behaviours (Heleniak & McLaughlin, 2020), meaning that deficits in understanding others' perspectives and emotions may contribute to outwardly-directed behavioural problems such as aggression or defiance. This suggests a nuanced relationship between socio-cognitive abilities and behavioural regulation, where challenges in recognising and interpreting social cues may hinder individuals' ability to navigate social interactions effectively.

Similarly, studies, link early childhood abuse to diminished outcomes in memory, executive functions, and attention assessments (e.g., Goltermann et al., 2021; Ainamani et al., 2021); and reduced inhibitory control (Xu et al., 2021). For example, Jacobsen et al. (2020), found that growing up in a foster homes was linked to reduced cognition. In their longitudinal study, they used the Weschler Intelligence Test for Children (WISC-IV) to measure the cognitive performance of participants. The WISC-IV is an individually administered assessment tool with fifteen subtests that together give a thorough assessment of intellectual capacity. It has norms for age 6-16 years (Williams et al., 2003).

Studies have shown that abuse and childhood adversity, have a pervasive effect on cognition, and the cerebral cortex in children living with HIV. Research indicates that exposure to abuse, neglect and other ACEs, leads to functional and structural changes in the cortex, especially in regions associated with cognitive processes such as memory, and attention (Kalia

& Knauft, 2020). Linked to the above, it is hypothesised that additional stressors, such as living in care shelters, which are associated with unstable living conditions, may have an effect on scholastic development (Rydström et al., 2019).

In summary, childhood adversity, (ACEs) negatively affect cognition and cerebral cortex integrity (Tryon et al., 2021). Noteworthy to my aims, ACEs disproportionally affect children living with HIV, leading to compromised neurocognition, amongst a population of the children (Holden et al., 2019) Notwithstanding, there is a death of literature detailing the effect of ACEs, children living with HIV, placed in HIV care shelters.

2.11. Biological sex, Ethnicity and Adverse Childhood Experience

Emerging research indicates that ACEs are unequally distributed in society based on sex , ethnicity, and economic status (Mersky et al., 2021b). In terms of biological sex, studies have indicated a higher incidence of ACE exposure among girls compared to boys (Almuneef et al., 2017 ; Fang et al., 2016; Leban, 2021). Among juvenile justice system youth, girls have been indicated to experience greater prevalence in ACEs compared to boys (29% vs 14%) (Sourander et al., 2016). Furthermore, compared to boys, girls tend to experience more sexual abuse (Mersky et al., 2021b), leading to distinct patterns of psychological and emotional sequelae such as depression, post-traumatic stress disorder (PTSD), and substance abuse.

A cross-national study by Koposov, and colleagues, (2021) explored sex disparities and exposure to community violence (CVE) in three countries, Belgium (n = 4,743), Russia (n = 2,823), and the US (n = 4,101) in connection to academic performance. Finding from in the study indicated that more girls than boys reported experiencing violent events (ranging from 37.4% to 51.6% between the countries) compared to boys. Experiences of violence were linked to poor educational outcomes regardless of the country's location (Koposov et al., 2021).

Similarly, Al Shawi et al. (2019), investigated the prevalence of ACEs among adults in Iraq, in relation to depression. Results from the Depression Anxiety and Stress Scales (DASS) indicated that 38.9% of males reported previous exposure to ACEs, while 61.1 % of females reported exposure. Greater exposure to ACEs amongst females was liked to increased levels of depression, with females experiencing greater levels of neglect, physical abuse, and sexual abuse (Al Shawi et al., 2019).

Similarly, Wang, (2023) examined biological sex -specific associations of ACEs with frailty indexes, from the China Health and Retirement Longitudinal Study. Findings indicated that over a lifetime, more females experienced greater ACEs than men. The biological consequences of early ACEs (childhood socioeconomic deprivation), in females were associated with heightened frailties, in old age (Wang, 2023). Similar outcomes were reported in a National Survey of Children's Health (NSCH), which indicated that for the most part, females between the ages of 6 and 17 years, experienced greater ACEs, than boys, resulting in females having a reduced ability to care about achieving better academic outcomes in schooling (Mcdowell, 2017).

Beside the above citations, other studies (e.g., Delisi et al., 2019; Giano et al. 2020; Schnarrs et al., 2019), have disproportionally reported greater levels of ACEs in females, than males. In such a study, Giano et al. (2020) provided updated estimates of ACEs using diverse sample in the United States. Consisting of a total of 211 376 adults, across 34 states, findings from the Risk Factor Surveillance System (BRFSS), which comprised eight measures of ACEs, : physical/emotional/sexual abuse, household mental illness, household substance use, household domestic violence, incarcerated household members, and parental separation/divorce, found that 57.8% of the sample experienced at least one ACE, and 21.5% experienced three or more ACEs (Giano et al., 2020). Females participants reported greater frequency of ACEs, with Black or Hispanic populations indicating greater ACEs, than

Caucasian descendants (Giano et al., 2020). Relevant to my research, the study found that those with higher incomes and higher levels of education, also experienced lower levels of ACEs.

2.12. Age and Adverse Childhood Experience

Although studies, seem to indicate that early life stressors (i.e., sexual abuse, poverty, low SES), are likely antecedents of cognitive, and behavioural consequences, and that females present with greater levels of ACEs, the effect of age group (children or adolescents), and its relation to ACEs, is not well undertook. Notwithstanding, in relation to age, research appears to indicate that the consequences of ACEs on cognition, depend on the frequency, type, and length, of ACEs experienced during the period from childhood to adolescence (Rovnaghi and Anand, 2018). Moreover, although early experiences of ACEs during childhood, result in cortical, and metabolic dysregulations, how it is not clear which age group (early childhood, early teen, early adolescence), experiences, the greatest levels of ACEs , what are the resultant effects on cognition or behavioural outcomes (Shonkoff et al., 2012). Nonetheless, this study will seek to understand this phenomenon by investigating the effect of ACEs in children living with HIV aged 10-16 years. Having established the effects of ACEs on sex, highlighting the limited understanding of ACEs, and age, the next section explores the effects of ACEs on individuals living with HIV.

2.13. Adverse Childhood Experiences and HIV

In addition to the effects of neuroHIV on cognition, adverse childhood experiences (ACEs), pose an added burden to children and adults living with HIV. Given the above, my research sought to investigate the cojoined nature of ACEs on HIV neurocognition. My study sought to investigate the effect of ACEs in a sample of children residing in HIV care shelter in South Africa. The study investigated the cojoined effect of ACE, and HIV, on attention skills. Attention was chosen as the cognitive domain of interest as research indicates that attention is the primary domain for learning and that other cognitive domains are superseded by attention.

Secondary to the above, attention and executive function decline are defining features of HAND (Antinori et al., 2015; Clifford and Ances, 2013; Heaton et al., 2011; Nichols et al., 2016). The subsequent section details the intersection of neuroHIV and ACE.

Lakkireddy et al. (2021) indicate that children and adults living with HIV are likely to experience ACEs. For example, Chenneville et al. (2022) investigated ACEs among HIV participants aged between 17-24 years (n=41). Findings from the study indicated that ACEs contribute to greater risk behaviours and are linked to negative health outcomes (Chenneville et al., 2022). ACEs in this population group were also linked to risk behaviour co-occurring with substance abuse disorder, which negatively affected medication adherence, poor health outcomes (Chenneville et al., 2022). In another study, Spies et al. (2016) examined the effects of childhood trauma on a sample of participants living with HIV. The study, inclusive of female participants, investigated the effects of childhood trauma on neurocognitive outcomes. The study was inclusive of HIV patients who either experienced early life stressors (ELS) (n=32), and those who did not (n = 30). Findings indicated that the right anterior cingulate cortex (ACC), bilateral hippocampi, corpus callosum, left and right caudate, and left and right putamen were shown to have significant group volumetric differences. When compared to all other categories, HIV-positive females with ELS, indicated lower mean regional volumes. Associated lower volumetric data on cortical regions, was associated with suboptimal neurocognitive performance in the areas related to processing speed, attention/working memory, and abstraction (Spies et al., 2019).

The authors conclude that childhood trauma may be a contributory factor to observed cortical alterations and subsequent neurocognitive decline within the sample. Research further highlights those participants living with HIV, who have experienced ACEs, present with mental health challenges. Young-Wolff et al. (2021) examined the association between ACEs, depression, and HIV-related outcomes, in a sample of 584 individuals living with HIV (Mean

Age =49.0; SD =10.9). The study found that most participants in their study were exposed to at least one ACE, and nearly half were exposed to three or more ACEs. In a similar study, Adeyemo et al. (2020), found the prevalence of ACEs, was high amongst children living with HIV in Lagos. As indicated by the Neuropsychiatric Interview for Children and Adolescents, 44.8% of participants presented with lifetime major depression, and 35% presented with suicidality (Adeyemo et al., 2020). Importantly, the study found a significant association between the prevalence of Adverse Childhood Experiences (ACEs) among children living with HIV in Lagos and the occurrence of mental health issues, as evidenced by high rates of lifetime major depression and suicidality (Adeyemo et al., 2020).

Moreover, the co-occurrence of ACEs and mental health disorders among children living with HIV suggests complex interactions between biological, psychological, and social factors that influence cognitive functioning and emotional well-being (Adeyemo et al., 2020). According to Adeyemo et al. (2020), there is a need to develop interventions, that address the holistic needs of children affected by HIV, and that these ought to foster resilience, and reduce the long-term effects of early-life stressors, on cognitive development.

In a South African study, Santoro et al. (2021) investigated the impact of adverse childhood experiences (trauma) on neurocognitive outcomes within a sample of 72 children and adolescents, recruited from HIV clinics in the Cape Metropolis region. Participants for the study (Female = 52.8%; Males = 47.2 %) were aged between the ages of 14-17 years. The study assessed cognitive function skills using the Trial Making Test (executive functions, working memory and attention), the Neuroscreen Number Speed Test (working memory), and the NEPSY-II (executive function). Childhood adversity was measured using the Adverse Childhood Experiences (ACE) scale (Santoro et al., 2021). Results indicated no significant differences by age or biological sex between individuals who experienced high levels of adversity (four or more measures) versus those who experienced low adversity (less than three

reports). Although no differences were found by age and sex, children in the study indicated poorer processing speed, working memory, and executive function outcomes.

The study by Santoro et al. (2021) highlights the association between ACEs and poor cognitive outcomes in children living with HIV in South Africa. Notwithstanding, the study had limitations in that it did not, (a) comprehensively investigate a singular cognitive domain (e.g., executive functions or attention), and the impact of ACEs, on this domain. The advantage of studying a single cognitive function in depth is that researchers can explore the complexities of different areas of cognition in a much greater detail. (Posner and Petersen, 1990). Furthermore, studying a single domain facilitates the identification and treatment of disorders that are specific to that domain, resulting in more successful therapeutic strategies that are adapted to the cognitive profile of the patient (Marquand et al., 2019). Additionally, researchers can create specialised interventions and therapies for problems with cognition or issues associated with attention skills deficits. Moreover, by focusing on a single cognitive domain of study, researchers can narrow down cognitive profiles (e.g., attention, working memory), by developing accurate assessments, or those profiles, based on behavioural or environmental contexts (Posner & Petersen, 1990).

Another limitation of the study, as highlighted by Santoro et al. (2021), is that their study (b) did not employ a validated measure, to investigate adverse childhood experiences, in individuals younger than 18 years of age. Simply stated, the authors utilised a measure validated for adult populations to assess ACEs, which could have affected study findings. Other than the limitations identified in Santoro et al. (2021), methodological limitations often affect the investigation of HIV/AIDS in South Africa, especially in relation to ACEs and cognition (Loggerenberg & Karim, 2008). Key limitations identified in the literature include, challenges accessing children living with HIV (Govender et al., 2012). Inability to access children, especially those living with HIV, and based in care homes, may invariably result in sampling

bias and underrepresentation of lived experiences of this population (Govender et al., 2012). As further noted by Simbayi et al. (2007), the fear of being discriminated against, or socially excluded, may result in children living with HIV, avoiding participating in research, or them not disclosing their status.

2.14. Summary of Reviewed Literature

The reviewed literature has indicated that neuroHIV affects cortical regions, such as the central executive network, and Posner's Attention Network, leading to HAND. Of relevance, the reviewed literature further indicates that HIV, affects attention skills in children. Moreover, childhood adversity has been linked with disturbed cortical morphology, leading to compromised neurocognition in children. Given the cojoined effect of ACEs, and HIV, on neurocognition, my study sought to address the dearth of intersectional research in paediatric HIV. To date, only one published study (i.e., Santoro et al. 2021) has investigated the impact of ACEs on neurocognition in children and adolescents living with HIV in South Africa. My research sought to add to this body of literature, by expanding on the early work of Santoro et al. (2021).

2.15. Study Objectives

The study expanded on the study by Santoro et al. (2021), by utilizing validated psychometric measures to assess childhood adversity experiences. In addition to the above, instead of focusing on multiple cognitive domains, my research investigated the effect of ACEs, on executive functions and attention. A secondary departure from Santoro et al. is that this study examined the specific role of demographic variables, namely, sex, age, and education on attention outcomes. These outcomes were related to High or Low levels of childhood adversity.

The study chose to focus on demographic variables, because, although the reviewed literature, indicates, that ACE outcomes, on cognition, differ by biological sex , ethnicity, age, and levels of ACEs experienced (High / Low) (e.g., Wamser-Nanney, 2018; Mersky et al., 2021; Slattery et al., 2022), there is conflicting findings regarding the magnitude and direction of these effects. Some studies suggest significant associations between specific demographic variables and cognitive outcomes following ACEs, while others report inconsistent or non-significant findings. This discrepancy underscores the need for further investigation and a more nuanced understanding of how demographic factors intersect with ACEs to influence cognitive functioning within the general population. Moreover, there was limited research on the effects of the above-mentioned variables, with a particular focus on children living with HIV, in HIV care shelters. Given this latter limitation, this study addressed, the gap by investigating the below research questions.

Research Questions:

Amongst children living with HIV and residing in Care Shelters:

a. Are there significant differences in attention outcomes based on the number of ACEs experienced?[5]
b. Are there significant differences in attention outcomes based on biological sex (females and males) based on adversity (Low vs High)?
c. Are there significant differences in attention outcomes based on schooling (primary and high school) based on adversity (Low vs High)?
d. Are there significant differences in attention outcomes based on age (young children: ages 10-13 years; and older children: ages 14-16 years), based on adversity (Low vs High)?

[5] As detailed in the Methods section, if a child experienced more than four ACES, this was deemed as High ACEs. If a child experienced three of fewer ACEs, this was deemed as Low ACEs.

CHAPTER 3: RESEARCH METHODOLOGY AND DESIGN

3.1. Research Methodology

This chapter describes the methods used in the study. This research study specifically sought to examine the effect of adverse childhood experiences (ACEs) on attention, as measured by the NEPSY-II. The research methods section is undertaken, considering multiple methodological challenges inherent in assessing children living with HIV within the African context. For example, Kvalsig and colleagues (2013) note that there are considerable methodological limitations that affect the investigation of HIV/AIDS research in Sub-Saharan Africa. Some of these, include researchers having to factor, (a) the influence of poverty on HIV outcomes; (b) impediments to accessing health care services, (c) developmental delays due to HIV, and (d) limitations of cARTs access to name a few. The above cited covariates all determine, and affect outcomes measures, regardless of the research methods undertaken to investigate the effect of HIV on neurocognition.

Notwithstanding the above cited factors, cultural variations within diverse populations within the continent, may inadvertently affect interpretation on neuropsychological performance within these samples. Also relevant to the study, genetic, and environmental factors may impact neuropsychological performance, over and above HIV diagnosis (Kvalsig,Taylor, Kauchali, and Chhagan, 2013). To mitigate some of the above complexities, the student researcher also a registered multilingual independent psychometrist (PMT0099694) conducted all neuropsychological assessments for the study using the participants' home language or the language of instruction, whenever necessary. For fidelity, the study used published NEPSY II norms for Afrikaans, Sepedi, Sesotho, Setswana, isiXhosa and isiZulu-speaking South African children (Truter, 2017) for scoring purposes. The published norms from Truter, (2017), take into account the effect of 'disadvantaged educational backgrounds' of children aged between 9 and 11 years of age, and those aged between 14 and 16 years of age

in scoring. The above age group correlate to children in Grades 4-6 and Grades 8-10, respectively (Truter, 2017).

3.2. Research Design

3.2.1. Design and Setting

This study took the form of a quantitative approach, which is defined as an empirical approach that employs numerical, quantifiable approaches to make conclusions regarding a phenomenon (Sullivan, 2012). The study took the form of a quantitative, descriptive, non-experimental research design. Such a design does not involve manipulating variables or randomizing groups but simply describes the nature of the phenomenon under investigation (Sullivan, 2012).

3.2.2. Dependent variables

A total of ten (10) attention and executive function measures from the *NEPSY-II* (*Section 3.4*) were used as the primary outcome variables for cognition. The assessments administered for attention and executive function were the Auditory Attention, Response Set, and Inhibition subsets of the NEPSY. Under *Auditory Attention* subtest, the dependent variables were Auditory Attention Total Scores, Auditory Attention Commission Total Errors, Auditory Attention Omissions Total, and the Auditory Attention Inhibitory Total. Dependent measures on *The Response Set* included Response Set Total Correct, Response Set Commission and Omission Errors Total. Finally, in the *Inhibition* subtest, the dependent variables were Inhibition Total Errors, Inhibition Naming Total Completion Time, and Inhibition Switching Total Completion Time.

3.2.3. Independent variables

The independent variable for my study were the reported ACEs, categorized into a binary of *High* and *Low* adversity. High adversity was represented by four (4) or more ACEs,

the participant may have been exposed to as determined by the *Adverse Childhood Scale*. Low childhood adversity was represented by three or less ACEs on the Adverse Childhood Scale (*Section 3.2.7*).

3.2.4. Setting

My research was carried out at two HIV shelters situated in Johannesburg, South Africa. The two shelters are registered non-profit organisations offering holistic care and support, to children living with HIV, and those orphaned. All children in the shelter permanently reside at the shelters and are under the care of a matron, social worker, and therapist. At the time of the study, all children lived at the shelter, and visited their relatives during school term holidays. In total, the two shelters accommodate approximately 185 children. Most children attend primary, secondary, and technical schools, within the surrounding environment of the shelters.

3.2.5. Participants

Convenient sampling was used to recruit forty-two participants from the two shelters. Research participants were aged between the ages of 10-16 years of age and were all on a course of ARVs at the time of the study. Sample size estimation for the research was based on the study by Santoro et al. (2021), who recruited 72 research participants from HIV clinics in Cape Town, South Africa. For my study, to achieve statistical power to answer the research questions under investigation, I considered an alpha = 0.05 and power = 0.80 for sample size estimation using G*Power 3.1 (2021). Based on G* Power estimation, it was deemed that for an adequate power of 0.8, forty-three (43) participants would be sufficient for the study to detect statistical differences for between group analysis (See Appendix A).

3.2.6. Inclusion and exclusion criteria:

The *inclusion criteria* for participant selection were that (1) participants should have resided at one of the two HIV care shelters, (2) and should have been diagnosed with HIV and

be on a course of ARVs. Lastly, participants (3) must be between the ages of 10 and 16 years of age. The *exclusion criteria* were participants who did not meet the above criteria and were previously involved in a similar research study within the last two years. Participants were also excluded if they presented with a significant diagnosis of neurological, psychiatric, or learning difficulty (as ascertained by the presiding nurse).

3.2.7. Measures

A ***Demographic Questionnaire*** (Appendix B) was administered to obtain participants'' data regarding HIV status, biological sex, age, and education. These variables are similar to those included in the Santoro et al. (2021) study. The parent/guardians or the Director of the shelter completed the Demographic Questionnaire.

Childhood Adversity: Childhood adversity data was captured using the Childhood Adversity Questionnaire (CYW ACE-Q: Burke Harris & Renschler, 2015). The CYW ACE-Q measures adversity as identified by variables such as (a) previous experience with long-term health challenges, (b) previous experience with learning difficulties, (c) previous experience with behavioural and mental health challenges, as well as (d) developmental delay before the age of 18 years.

Further to the above, the CYW ACE-Q is comprised of two sections: Section 1 of the instrument (items 1–10) measured childhood adversity based on illness risk profile. Section 2 (items 11–20) assessed early life stressors linked to adversity, such as being placed in a foster care system, experiencing bullying, losing a parent or guardian, experiencing deportation or migration, or experiencing trauma due to a medical condition, and being exposed to violence and/or discrimination (Burke Harris & Renschler, 2015). Where appropriate, research participants completed the questionnaire (Appendix C), but, for the most part, these were completed by the caregivers (Appendix D).

The psychometric properties of the CYW ACE-Q are well attested, and include adequate internal and external validity (Lanier et al., 2018). The instrument has also been found to demonstrate adequate test–retest reliability and concurrent validity (Bethell et al., 2017; Choi et al., 2020; Hardcastle et al., 2018; Sherr et al., 2016). According to Lamers et al. (2011), the CYW ACE Q has a good internal consistency reliability with a Cronbach's alpha coefficient of 0.70 for the total scale. To date, although appropriate for the age groups in the study, the instrument is yet to be normed and validated within a South Africa context.

***Attention and Executive Functions*:** Neuropsychological data from the NEPSY-II was administered to assess neurocognitive function. The NEPSY-II is a multidomain neuropsychological battery that evaluates pre-schoolers, children, and teenagers'' neurocognitive abilities (Korkman, Kirk, and Kemp, 2007). The NEPSY-II captures cognitive data pertaining to (a) attention and executive functions, (b) language, (c) memory and learning, (d) social perception, (e) sensorimotor skills, and (f) visuospatial processing. For this study, I focused on data related to subcomponents of attention, specifically executive and sustained attention. Psychometric properties of the NEPSY include good internal reliability ($r \geq 0.80$) and content validity ($r = 0.51$ - 0.96). Due to its reliability and validity, the NEPSY II has previously been used in several Sub-Saharan African settings, including, but not limited to South Africa (Louw et al., 2020; Semrud-Clikeman et al., 2017), Zambia (Roy, 2018; Mulenga et al., 2001), and Botswana (Korkman, and Kirk, 2007). Although Cronbach's alpha values for the NEPSY-II subtests, vary depending on the age group and the population being studied (Korkman, and Kirk, 2007)., the NEPSY-II has been demonstrated to have good internal consistency across multiple subtests. For instance, in a study by Korman and Kemp, (2007) which evaluated the psychometric properties of the NEPSY-II in a sample of children aged 3-16 years, the Cronbach's alpha coefficients, for individual subtests ranged from 0.43 and 0.90, with most subtests showing acceptable levels of internal consistency. Specifically, for the

Auditory Attention and Response Set subtest, the internal consistency coefficient (Cronbach's alpha) was reported to be 0.86, (Korkman et al.,2007), whilst the Comprehension of Instruction, Design Copying, Geometric Puzzles, Inhibition, Speeded Naming, and Word List Interference, indicated alpha coefficients ranging from 0.70 to 0.90. All these indices (Korkman et al.,2007) indicate good reliability across individual subtests (Korkman, Kirk, & Kemp, 2007).

The following subtests from *NEPSY-II* ((Korkman et al.,2007) were administered to collect data on attention and executive functions.

***Auditory Attention and Response Set*.:** This subtest uses an auditory continuous performance paradigm to measure selective and sustained attention, response inhibition, and executive functioning. Two components comprise this subtest: *Auditory Attention* is designed to assess selective sustained auditory attention. It evaluates the capacity of participants to sustain and selectively attend to auditory attention. The *Response Set*, on the other hand, evaluates a participant's capacity to switch to and retain a new, more complex mental set in their mind. The task further demands participants to multitask in working memory, and to inhibit the impulse to respond in the same way as in Auditory Attention, or in accord with visual stimulus. In this task, the participant needs to pay close attention, monitor responses for rule violations and inhibit immediate impulse. When the participant hears a target word in a string of words, they touch a relevant circle target. Furthermore, the participant must react quickly, which may increase impulsive reactions, leading to errors of commission. Thus, the Response Set requires more executive control than Auditory Attention due to the cognitive load and working memory requirement of the task (Korkman & Kirk, 2007).

Comprehension of Instructions: This task assesses participant's ability to comprehend, interpret, and apply spoken instructions of increasing syntactic complexity. In response to spoken directions, the participant points to rabbits of different sizes, colours, and facial

expressions. Furthermore, more complex items involve pointing to shapes by colour, position, and relationship to other figures (Korkman et al.,2007).

Design Copying: The subtest is designed to assess visuoconstructional ability and visuomotor integration. This measure assesses the participant's ability to perceive and analyse the visual-spatial relationships in the design, and retain the image by copying the figures displayed in the response booklet (Korkman et al.,2007).

Geometric Puzzles: The subtest is intended to assess mental rotation, visuospatial analysis and attention to detail. The participant is presented with a picture of a large grid containing several shapes, and they are expected to analyse and compare the geometric aspects of the figures to perform this task (Korkman et al.,2007).

Inhibition: The Inhibition subtest was designed to assess multiple aspects of executive functioning, including inhibitory control, cognitive flexibility and self-monitoring. In this task, depending on the colour of the shape or arrow, the participant labels either the shape, the direction or a different answer when presented with a sequence of black and white shapes or arrows (Korkman et al.,2007).

Speeded Naming: This subtest is intended to evaluate participants'' ability to rapidly access and produce names, colours, forms, sizes, or letters and numbers. Participants must name items as rapidly as possible in the order they appear in the NEPSY-II stimuli book (Korkman et al.,2007).

Word List Interference: The subtest measures verbal working memory, repetition, and interference-induced word recall. The participant is given a two-word series and instructed to repeat each sentence once it is given. Then, in the presentation order, he or she recalls each word series as per the word list (Korkman et al.,2007).

3.2.8. Procedure

Upon approval of the study by the Rhodes University Human Research Ethics Committee (Appendix E), the Directors of the two shelters were sent letters requesting permission to conduct the study at their premises. Following Director approval, further approval was sought from parents/guardians to provide consent for their ward to partake in the study (Appendix F). Once children provided assent (Appendix G), data collection commenced.

On the day of the research, all data collection was conducted in a well-ventilated and quiet room allocated to the researcher by the respective HIV care shelters. Each room had sufficient space and lighting and was furnished with chairs and a desk. Participants were first presented with a *Demographic Questionnaire* to confirm relevant demographic data (i.e., child's birthdate, age, level of education, etc). In cases where children could not provide demographic data, the Directors, matrons, or care givers provided such data. Once complete, participants proceeded to complete the *CYW ACE-Q,* which took approximately 15 minutes to complete. Similarly, in cases where children could not provide ACE data, the Directors, matrons, or care givers assisted with relevant information.

Once the above phases were complete, participants were then administered the *NEPSY-II* subsets described above. Administration of the *NEPSY* took approximately two and a half hours per child to complete, with intermittent breaks of approximately five-minutes between assessments.

Data collection for the study was conducted between July 2022 to November 2022. All data was collected after school hours (i.e.,14h30 to 17h00), during weekdays (Monday to Friday). Occasionally, data collection was conducted on weekends (Saturdays between 08h00 to 16h00) based on participant availability. Procedurally, after school, when participants had taken lunch, each participant would meet the researcher in the room allocated for the study and be briefed about the study proceedings. Once data collection was complete, participants were thanked for their participation and given a token of appreciation.

3.2.9. Data Management and Data Analysis

Descriptive analysis: All data (Demographic, ACE, NEPSY) were transferred into Excel and then saved on the cloud. Once data cleaning was complete, basic descriptive analysis were conducted in the form of frequency analysis (Demographic analysis) and assumption checks were run on all dependent measures. Significantly, continuous data from the *CYW ACE-Q* were transformed into categorical data denoting *High* (four or more ACEs) and *Low* (four or less ACEs) Adversity. These transformations were implemented, to enable further regression analysis on the outcome variables of interest (NEPSY: Attention scores: *Auditory Attention*, *Response Set*, and Inhibition subtest). All data transformations, and subsequent analysis were conducted on Jamovi 2.3.21 statistical package (The Jamovi project (2022). For all statistical analysis, the level of significance was set at the alpha level of $p < 0.05$.

Age:

According to Piaget, cognitive development occurs in phases, each of which is distinguished by unique cognitive capacities and worldviews (Piaget, 1952). The first stage is the sensorimotor stage. This is the initial stage where infants aged (0-2 years) learn about the world through their sensory experiences and motor actions. The key developments in this stage include object permanence and the coordination of sensory and motor experiences. The second stage is the Preoperational stage. During this phase, children begin to use language in engage in symbolic play, however, they do not yet understand concrete logic. They show egocentric behaviour , that is having difficulty seeing things from perfective other than their own and struggle with concepts of conversations (e.g., the understanding that the quantity of liquid remains the same regardless of the shape of the container, the idea that the number of objects remains constant despite changes in their arrangement, and the recognition that the volume of clay remains unchanged even if its shape is altered). This stage is followed by the Concrete operational stage (7-11 years). This phase is characterised by children starting to think logically

about concrete events. They gain a better understanding of the concept of conservation, perform operations on concrete objects, and understand the concept of reversibility. They begin to grasp mathematical concepts and categorise objects (e.g., understanding the principles of addition and subtraction, recognizing that the total number of items in a set remains the same despite rearrangement, classifying objects into hierarchical categories based on shared characteristics, and comprehending the concept of conservation, such as recognizing that a volume of liquid remains constant despite changes in the shape of the container)

The sample was split into two age bands. The age categorization in this study was grounded in the cognitive development psychology theory of Piaget'. According to Piaget's cognitive development theory, cognitive development occurs in phases, each of which is distinguished by unique cognitive capacities and worldviews (Piaget, 1952). There are various reasons why dividing a sample into two age groups is consistent with Piaget's theory. Firstly, are developmental differences. Piaget argued that cognitive development occurs in different phases consisting of sensorimotor, preoperational, concrete operational, and formal operational. This made it possible to compare the cognitive ability of children who are more likely to be in the formal operational stage and children who are more likely to be in the preoperational or concrete operational stages by dividing the sample into two age bands. The two groups fell in the concrete operational stage (7-11 years), and the formal operational stage (12 years and up) This division also made it possible to investigate how cognitive abilities change as children progress through Piagetian stages.

3.2.10. Inferential Analyses

Correlation: Correlation analyses were conducted between ACEs and attention scores (Auditory Attention, Response Set, and Inhibition subtest), using Pearson's Correlation Matrix. Furthermore, Chi-square measures of association were conducted on categorical data (High vs

Low Adversity), between ACEs and attention scores (Auditory Attention, Response Set, and Inhibition subtest).

T-Test Analysis: Independent sample T-Tests were conducted to test group difference by sex (male, female), adversity (high and low-adversity), on attention and executive function outcomes.

Linear Regression: Linear regression analysis was conducted to determine the relationship between ACEs measures and attention /executive outcomes. The effect of ACE on attention scores was analysed using a hierarchical regression analysis.

3.2.11. Ethical considerations

Ethical clearance for the larger NRF study was granted to the Principal Investigator (research supervisor) (Appendix H). Ethical clearance for the Masters study was granted by the Rhodes University Human Research Ethics Committee (RU-HREC: 2022-5149-6934). Given the sensitive nature of the research (HIV children), all participant information data was treated with strict confidentiality in accordance with the POPIA Act (Republic of South Africa, 2013). As such, to ensure confidentiality and anonymity, subject codes were assigned to each participant. All participant information was kept private and stored in a safe and secure location only accessible to the researcher and the research supervisor. The study followed the Helsinki Protocol of Ethics (World Medical Association, 2014), wherein, participants were protected from harm by ensuring they had access to counselling services at the child centre. Participants were further informed that they had a right to discontinue the study at any time without any consequences. Importantly, parents, guardians and participants were briefed of the voluntary nature of the study, and children provided informed assent both in writing and verbally.

This study was conducted during the surge of COVID-19 infections. To mitigate risk of COVID-19 infections, a risk mitigation plan was implemented, to which participants and the researcher had to adhere (Appendix I).

CHAPTER 4: RESULTS

4.1. Descriptive Statistics

Table 1 captures the demographic characteristics of the sample. In total, 42 participants took part in the study. Males constituted 52.4 % (n=22), whereas females constituted 47.6% (n=20) of the sample. The mean average age was (M = 14.5 years, SD = 1.90), and the majority of participants reported being Black (88.1%), with the least number of participants being White (2.4%). Most participants were in High School, (81%), with 8 (19%) participants in Primary School. Participants spoke a variety of languages, with isiZulu (46%), being the most widely spoken language. All participants were fluent in English, and all assessments were conducted in English, or the child's home language when appropriate. Chi- Square Analysis revealed no significant differences by and sex and Education, χ^2 (1) = 0.02, p = 0.88. Similarly, no differences were found by sex and ethnicity, χ^2 (1) = 5.59, p = 0.061. The subsequent section presents descriptive statistics for ACE scores.

Table 1

Demographic Sample Characteristics

Sample Characteristics	(N)	(%)
Age		
Age categorised (Young and Old)	30	71.4
Young participants (10-13)	12	28.6
Old participants (14-16)	30	71.4
Sex		
Female	20	47.6
Male	22	52.4
Ethnicity		

Black	37	88.1
Coloured	4	9.5
White	1	2.4
Level of education		
High school	34	81
Primary school	8	19
ACEs		
High adversity	31	73.8
Low adversity	11	26.2

Note. N= Frequency of participants in each category. % = Percentage of participants in each category.

4.2. Adverse Childhood Experiences (ACEs)

Descriptive statistics for ACE scores based on High and Low adversity are presented in Table 2. As indicated in Table 2, no significant differences were noted between males (M = 9.07, SD = 2.50) and females, (M = 9.65, SD = 3.14) on the number of ACEs, an individual experienced. As further indicated in Figure 1, approximately 14 (33.3%) participants reported having experienced ten or more ACEs on the CYW-ACE-Q. Furthermore, 12 participants (28.6%) reported having experienced 4-6 ACEs, with a further 10 (23.8%) reporting at least seven or more ACEs. Moreover 6 participants (14.3%) reported experiencing at least one to three ACEs. Overall, 73.8% of participants (n = 31) reported having experienced 'High' Childhood Adversity, as indicated by the CYW ACE. Conversely, 26.2% participants (n = 11) experienced 'Low Childhood Adversity'. On average, the sample experienced at least 7.67 (8) ACEs, with a standard deviation of 3.85 (4).

Table 2

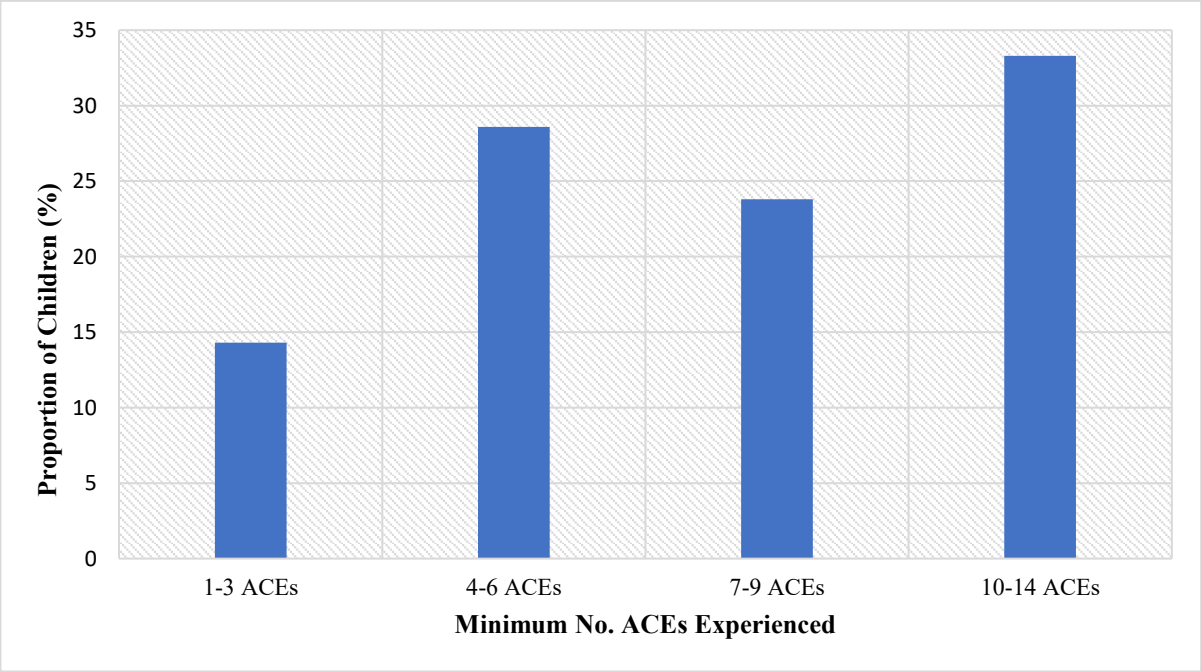
Descriptive Characteristics of Adverse Childhood Adversity

Measure	Female		Male		Full sample	
	Mean	Standard deviation (SD)	Mean	Standard deviation (SD)	Mean	Standard deviation (SD)
ACEs						
High Adversity	9.65	3.14	9.07	2.50	9.39	2.84
Low Adversity	3.67	0.58	2.50	1.31	2.82	1.25

Note: High and Low number of adversities in females and males are represented in mean and standard deviation (SD).

Figure 1

The Number of Children living with HIV and have Experienced ACEs



Note: The numbers of ACEs experienced by each participant are categorised from minimum to maximum ACEs experienced.

4.3. Inferential Statistics: Research Questions

4.3.1. Research Question One

The first research question sought to answer the question: Are there significant differences in attention outcomes amongst children living with HIV, who have experienced a greater number of ACEs (four or more), compared to those who have experienced fewer ACEs (three or less)?

Independent sample T-Tests analysis revealed no significant effect for adversity (High vs Low), on multiple measures of attention, namely, Auditory Attention Total Scores, Response Set Total Correct Scores, Response Set Commission and Omission Errors ($p > 0.05$). Similarly, no significant differences were found concerning adversity (High vs Low), and Auditory Attention Omissions Total Scores, Inhibition Total Errors scores and Inhibition Naming Total Completion Time. Nonetheless, children with High ACEs performed significantly worse (M =1.065, SD =1.41), for Auditory Attention Commission Total Errors compared to those with Low levels of adversity (M=0.182, SD=0.603), t (40) = 9.01, p = 0.05. Significant differences were also noted for Auditory Attention Inhibitory Total Scores, with participants who experienced Low ACEs, performing better (M=0.00, SD=0.00) than those who experienced a greater number of adversities (M=0.806, SD =1.33), t (40) = 7.79, p = 0.05.

4.3.2. Research Question Two

The second question sought to answer the question: Are there significant differences in attention outcomes by sex (females and males) based on adversity (low vs high)? A hierarchical regression analysis was conducted with two blocks (models) of variables. As indicated in Table 3, the first model included ACEs (High vs Low adversity), as the first predictor variable, with NEPSY-II outcome scores for attention (*Auditory Attention Total Scores*) as the outcome variables. In the second model, sex was included as a predictor, to investigate the effect of sexsex on the outcome variable (Auditory Attention Total scores). Results indicated that the

first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=1.49, p=0.23, R^2 =0.04), and explained 4% of the variation on outcome scores. Further coefficient analysis, although insignificant (p = 0.14), indicated that, for the variable 'Low Adversity', for every unit change in Low adversity, there was a decrease of 0.93 units in attention scores (*Auditory Attention Total Scores*). When sex was added as a covariate, the model was statistically significant (F=3.23, p=0.05, R^2=0.14). Importantly, the second model showed significant improvement from the first model ΔF = 4.83, p =0.03, ΔR^2= 0.11. Summarily, when ACEs (High vs Low), and sex (Male and Female), were included into the model, the model was able to explain 14.2 % of the variance in attention scores (AA total scores). Further, significant beta coefficient analysis of the regression model (p = 0.041) indicated that females (M = 2.25, SD = 1.8) performed significantly better than males (M = 1.05, SD = 1.36) on *Auditory Attention Scores*, t (35.25) = 2.42, p = 0.021.

Further to the above, a hierarchical regression analysis was conducted with two blocks (models) to study outcomes on Auditory Attention Commission Errors Total scores. In the first model, ACEs (High vs Low adversity) were included as the first predictor, with NEPSY-II outcome scores for attention (*Auditory Attention Commission Errors Total*) as the outcome variable. sex was then added as a predictor variable in the second model, to measure its effect on attention scores (*Auditory Attention Commission Errors Total*). Overall results indicated that although the first model (High vs Low Adversity) approached significance, it was an insignificant predictor for attention scores, (F=3.98, p=0.05, R^2 =0.09), and explained 9.1% of the variation in attention scores. Coefficient analysis was found to be significant (p = 0.05) and indicated that for the variable 'Low Adversity', for every unit change in the Low adversity, there was a decrease of 0.85 units in attention scores. As indicated in Table 3 for the second model, when l sex was added as a covariate, the model was statistically significant (F=4.63, p=0.02, R^2=0.19). Importantly, the second model showed significant improvement from the

first model $\Delta F = 4.90$, $p = 0.03$, $\Delta R^2 = 0.10$. Summarily, when ACEs (High vs Low), and sex (Male and Female), were included into the model, the model was able to explain 19.2% of the variance in attention scores (Auditory Attention Commissions Errors Total). Further, significant beta coefficient analysis of the regression model ($p = 0.03$) indicated that females ($M = 1.35$, $SD = 1.46$) performed significantly better than males ($M = 0.36$, $SD = 0.95$) on the outcome variable, *Auditory Attention Commission Errors Total*, t (39) = 1.45, $p = 0.03$.

A hierarchical regression analysis was also conducted with two blocks (models) to investigate attention scores (*Response Set Total Correct*) by ACE and sex. The first model included ACEs (High vs Low adversity) as the first predictor, with NEPSY-II outcome scores for attention (*Response Set Total Correct*) as dependent variables. In the second model, sex was included as a predictor variable, to the dependent variable (*Response Set Total Correct*). Results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=0.18, p=0.68, R^2 =0.00), and explained 0% of the variation in attention scores. Further coefficient analysis, although insignificant ($p = 0.67$), indicated that, for the variable 'Low Adversity', for every unit change in Low adversity, there was a decrease of 0.21 units in attention scores. For the second model, when sex was added as a covariate, the model was statistically significant (F=3.51, p=0.04, R^2=0.15). Importantly, the second model showed significant improvement from the first model $\Delta F = 6.81$, $p = 0.01$, $\Delta R^2 = 0.15$. Summarily, when ACEs (High vs Low), and sex (Male and Female), were included into the model, the model explained 1% of the variance in attention scores (Response Set Total Correct). Further, significant beta coefficient analysis of the regression model ($p = 0.013$) indicated that females ($M = 2.00$, $SD = 1.46$) performed significantly better than males ($M = 0.91$, $SD = 1.27$) on the outcome variable, *Response Set Total Correct*, t (39) = 1.79 $p = 0.013$.

Lastly, a hierarchical regression analysis was conducted with two blocks (models) of variables. Similar to the previous analysis, the first model included ACEs (High vs Low

adversity) as the first predictor, with *NEPSY-II* outcome scores for attention (*Response Set Commission Errors Total*) as the dependent variable. In the second model, sex was included as the second predictor variable, to determine outcomes on *Response Set Commission Errors*. Results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=0.00, p=0.95, R^2 =0.00), and explained 0% of the variation in scores. Coefficient analysis, although insignificant (p = 0.14), indicated that, for the variable 'Low Adversity', for every unit change in the Low adversity, there was a decrease of 0.24 units in attention scores. When sex was added as a covariate, the model was statistically insignificant (F=0.30, p=0.74, R^2=0.02). As indicated in Table 3, the second model showed insignificant improvement from the first model ΔF = 0.59, p = 0.47, ΔR^2= 0.01. Summarily, when ACEs (High vs Low), and sex Biological Male and Female), were included into the model, the model was able to explain 12.2 % of the variance in attention scores (Response Set Commission Errors Total). Significantly, beta coefficient analysis of the regression model indicated that females (M = 1.80, SD = 1.44) performed significantly worse than males (M = 2.14, SD = 1.40), on the outcome variable, *Response Set Commission Total Errors*, t (39) = 2.05, p = 0.001.

Table 3

Hierarchical Regression Analysis for Biological sex

Variables	R	ΔR^2	F	*p*
AA total scores				
Model 1 -ACEs (High vs Low Adversity)	0.19	0.04	1.49	0.23
Model 2 (Biological sex)	0.377	0.14	3.23	0.05
AA commission errors total				
Model 1-ACEs (High vs Low Adversity)	0.30	0.09	3.98	0.05

Model 2 (Biological sex)	0.438	0.19	4.63	0.02
Response Set total correct				
Model 1-ACEs (High vs Low Adversity)	0.07	0.0	0.18	0.70
Model 2 (Biological sex)	0.39	0.15	3.50	0.04
Response Set omissions errors total				
Model 1-ACEs (High vs Low Adversity)	0.08	0.00	0.24	0.63
Model 2 (Biological sex)	0.48	0.23	5.73	0.01

Note. The scores of the *NEPSY-II* subtests are presented by the adversity group. In each subtest, Model 1 represents High vs Low Adversity, and Model 2 represents the addition of sex.

4.3.3. Research Question Three

The third question sought to answer the question: Are there significant differences in attention outcomes between Primary and High school children based on adversity (Low vs High)?

A hierarchical regression analysis was conducted with two blocks (models) of variables. The first model included ACEs (High vs Low adversity) as the predictors, with NEPSY-II outcome scores for attention (*Response Set Total Correct*), as the dependent variable. In the second model, the Level of education was included as a predictor variable (Primary vs High School), to the dependent variable, to measure its effect on attention scores. Overall results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=0.18, p=0.63, R^2 =0.0), and explained 4% of the variation in attention scores. Further coefficient analysis, although insignificant (p = 0.68.), indicated that, for the variable Low Adversity, for every unit change in Low Adversity, there was a decrease of 0.21 units in attention scores. For the second model, when Primary and Secondary education were added as a covariate, the model was statistically insignificant (F=0.54, p=0.60, R^2=0.03). Although the second model showed improvement from the first model, ΔF = 0.89, p = 0.35, ΔR^2= 0.02, it remained insignificant. Summarily, when ACEs (High vs Low), and Level of

Education (Primary and High School), were included into the model, the model explained 3% of the variance in attention scores (Response Set Total Correct). Contrary to expectation, beta coefficient analysis of the regression model (p = 0.67) indicated that Primary School participants (M = 1.00, SD = 1.41) performed significantly better than High School participants (M = 1.53, SD = 1.1.42) on the outcome variable, Auditory Attention Scores, t (39) = 2.42, p = 0.01.

As indicated in Table 4, another hierarchical regression analysis was conducted with two blocks (models) of variables. Similar to the above analysis, in the first model, ACEs (High vs Low adversity) was added as the first predictor, with NEPSY-II outcome scores for attention (*Response Set Omissions Error Total*), as dependent variables. In the second model, Level of education was included as the second predictor variable, to the dependent variable (*Response Set Omission Errors Total*). Results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=0.24, p=0.63, R^2 =0.0), and explained 0% of the variation in attention scores. Further coefficient analysis, although insignificant (p = 0.63), indicated that, for the variable 'Low Adversity', for every unit change in the Low adversity, there was a decrease of 0.24 units in attention scores.

When the second model was added as a covariate, the model was statistically insignificant (F=0.62, p=0.54, R^2=0.03). Although, the second model showed insignificant improvement from the first model (ΔF = 1.00, p = 0.32, ΔR^2= 0.02), when Level of Education was added, the model explained 3 % of the variance in attention scores (Response Set Omissions Errors Total). Beta coefficient analysis of the regression model indicated that Primary School participants (M = 1.00, SD = 1.41) performed significantly better than High School participants (M = 1.56, SD = 1.36) on the outcome variable, *Response Set Omissions Errors Total*, t (39) = 2.04, p =0.00.

Table 4

A Hierarchical Regression Analysis for Education

Variables				
	r	ΔR^2	F	*p*
Response Set total correct				
Model 1-ACEs (High vs Low Adversity)	0.06	0.00	0.18	0.68
Model 2 (Education)	0.17	0.02	0.53	0.59
Response Set omissions errors total				
Model 1-ACEs (High vs Low Adversity)	0.08	0.00	0.24	0.63
Model 2 (Education)	0.18	0.03	0.61	0.54

Note. The scores of the *NEPSY-II* subtests are presented by adversity group. In each subtest, Model 1 represents High vs Low Adversity, and Model 2 represents the addition of level of education.

4.3.4. Research Question Four

In a follow up to the above findings, (primary school participants performing better than high school participants, on the *Response Set Omissions Errors Total* attention scores), Question Four investigated whether there are significant differences in attention scores, between younger (ages 10-13 years) and older children (ages 14-16 years), by adversity (Low vs High)?

Hierarchical regression analysis was conducted with two blocks (models) of variables. The first model included ACEs (High vs Low adversity) as the predictor variable, with NEPSY-*II* outcome scores for attention (Auditory Attention Omission Total Errors) as dependent variables. Age was included as a predictor variable, to the dependent variable (Auditory Attention Omissions Total Errors) to measure its effect of attention. Although approaching significance, results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=2.96, p =0.06, R^2 =0.08), and explained 8 % of the variation in Auditory Attention Omission Total Error scores. Further coefficient analysis, although insignificant (p = 0. 07), indicated that, for the variable 'Low Adversity', for every unit change in Low adversity, there was a decrease of 1.20 units in attention scores. When age was added onto the model, the model was statistically significant (F=4.47, p =0.02, R^2 =0.19). Importantly, the second model showed significant improvement from the first model $\Delta F = 5.08$, $p = 0.03$, $\Delta R^2 = 0.11$. Summarily, when ACEs (High vs Low), and Age (Old and Young), were included into the model, the model was able to explain 18.6 % of the variance in Auditory Attention Omissions Errors Total scores. Beta coefficient analysis of the regression model (p = 0.07) indicated that older participants (M = 0.70, SD = 1.29) performed significantly worse than younger participants (M = 1.17, SD = 1.34) on Auditory Attention Omissions Errors Total scores, t (39) = 2.67, p = 0.001.

Further hierarchical regression analysis was conducted with two blocks (models) of variables. The first model included ACEs (High vs Low adversity) as the first predictor, with NEPSY-II outcome scores for attention (Response Set Commissions Total Errors) as the dependent variable. In the second model, Age was included as a predictor variable, to the dependent variable (Auditory Attention Omissions Total Errors) to measure its effect on Response Set Commissions Total Error attention scores. Results indicated that the first model (High vs Low Adversity) was an insignificant predictor for attention scores, (F=0.00, p= 0.95,

R^2 =0.01), and explained 0% of the variation in outcome scores. Coefficient analysis, although insignificant (p = 0. 069), indicated that, for the variable Low Adversity', for every unit change in the Low adversity, there was a decrease of 1.39 units in attention scores. In the second model, when Age was added as a covariate, the model was statistically significant (F= 4.90, p=0.01, R^2=0.20). Importantly, the second model showed significant improvement from the first model $\Delta F = 4.90$, p= 0.01, ΔR^2= 0.45. Summarily, when ACEs (High vs Low), and age (10-13 years), (14-16 years) were included into the model, the model explained 3% of the variance in Response Set Omission Total Error scores. Beta coefficient analysis of the regression model (p =0.003) indicated that older participants (M = 1.60, SD = 1.43), performed significantly better than younger participants (M = 1.08, SD = 1.38) on the outcome variable, Response Set Omissions Total Errors, t (39) = 1.66, p = 0.00.

Table 5

A Hierarchical Regression Analysis for Age

Variables				
	R	ΔR^2	F	p
AA commission errors total				
Model 1-ACEs (High vs Low Adversity)	0.28	0.08	3.50	0.07
Model 2 (Age)	0.43	0.19	4.47	0.02
Response Set omissions errors total				
Model 1-ACEs (High vs Low Adversity)	0.08	0.01	0.24	0.63
Model 2 (Age)	0.18	0.03	0.63	0.54
Response Set commissions errors total				

Model 1-ACEs (High vs Low Adversity)	0.01	0.00	0.00	0.95
Model 2 (Age)	0.45	0.20	4.90	0.01
Response Set inhibitory total				
Model 1-ACEs (High vs Low Adversity)	0.20	0.04	1.70	0.20
Model 2 (Age)	0.32	0.10	2.17	0.13
Inhibition total time completion				
Model 1-ACEs (High vs Low Adversity)	0.03	0.00	0.03	0.86
Model 2 (Age)	0.26	0.07	1.40	0.26

Note. The scores of the *NEPSY-II* subtests are presented by adversity group. In each subtest, Model 1 represents High vs Low Adversity, and Model 2 represents the addition of Age.

CHAPTER 5: DISCUSSION

While persons living with HIV have benefited from advances in the development of ARV therapy, patients living with HIV continue to experience HIV associated neurocognitive disorders (HAND), partly due to ARV neurotoxicity, and limited ARV penetrance into the CNS (Boivin et al., 2019; Koekkoek et al., 2008; Lowenthal et al., 2014). HAND is further compounded by external factors such as environmental context, and childhood adversities (ACEs). ACEs have been noted to negatively impact mental health and HIV outcomes (Young-Wolff et al., 2019). Significantly, research indicates, that cognitive functions such as attention and executive functions, observed in HAND, are heightened by the experience of ACEs (Zelazo & Carlson, 2020). Surprisingly, there has been limited research investigating the intertwined nature of HAND (attention and executive function), and the effect of ACEs, in HIV neurocognition.

Given the above limitations, the primary purpose of my study, was to expand on early findings by Santoro et al. (2021), by investigating the impact of ACEs, on a single cognitive domain, namely, attention. As previously stated, the advantage of investigating a single cognitive domain is that facilitates the identification and treatment of disorders that are specific to that domain, resulting in more successful therapeutic strategies that are adapted to the cognitive profile of the patient (Marquand et al., 2019) Additionally, researchers can create specialised interventions and therapies for problems with cognition or issues associated with attention skills domains.

Additionally, understanding the domain of attention can serve as a framework for future interdisciplinary research and can be used as a foundation for multidisciplinary studies in the future (Posner & Petersen, 1990). The current study was thus premised on the central hypothesis, that experiences of early childhood adversity, profoundly affect neurocognitive

outcomes. The below sections summarise and discuss the study findings in light of the reviewed literature.

5.1. Summary of Key Findings

5.1.1. Adverse Childhood Experiences and Demographic Variables

Research Question One

Previous research (e.g., Goldstein et al., 2021) has indicated that outcomes in adverse childhood experiences (ACEs), are mediated by multiple variables including the frequency of ACEs, sex, income, and ethnicity. The first research question sought to investigate whether there were significant differences in attention outcomes, based on children's experiences of higher ACEs (four or more), or fewer ACEs (three or less). Findings from the study indicated that participants who experienced a high number of ACEs (four or more), performed significantly poorly on multiple attention subtests, compared to those who experienced a fewer number of ACEs (three or less). Findings from this study are similar to those reported by Santoro et al. (2021). In their study, Santoro et al. found that differences in ACEs (High vs Low) explained 10 –19% of the variation in outcome scores related to executive functions, and processing speed, with those experiencing a higher number of ACEs, performing significantly worse on these cognitive measures.

Similarly, Guinosso et al. (2016) investigated the effect of adverse childhood experiences on cognitive development and found that child adversity (e.g., experiencing child abuse, parental substance abuse), was linked with diminished outcomes in childhood verbal skills, attention and working memory abilities. The authors however noted that children who experienced less adversity, maintained optimal and constant cognitive abilities throughout through adolescence, extending to their schooling years (Guinosso et al., 2016).

Similar findings indicating that higher levels of ACEs lead, to cognitive decline in children, have been reported in African samples. For example, Amene et al. (2023), assessed the frequency of ACEs in five sub-Saharan African countries with low and intermediate incomes. Data from the Violence Against Children and Youth Surveys (VACS) (Ages 18 -24) conducted in Cote d'Ivoire (2018), Kenya (2019), Lesotho (2018), Mozambique (2019), and Namibia (2019) (n = 8766 girls and 2732 men), indicated that males experienced high numbers of ACEs (n=3 or more) when compared to females. Despite the above, a higher prevalence of sexual violence was reported in females and this was associated with poorer cognitive outcomes, and lower levels of educational attainment amongst females (Amene et al., 2023).

In another study, Wang et al. (2023) investigated the effects of ACEs on cognitive function in Chinese middle-aged individuals. The study found that unfavourable childhood experiences, namely in health, were associated with adverse cognitive outcomes in later life. From the reviewed studies, the most important conclusion about the effects of high and low levels of adversity on cognition is that ACEs (adverse childhood experiences) significantly affect cognitive functioning. These studies revealed that people who encountered higher levels of adversity as children frequently displayed worse cognitive outcomes in comparison to people who experienced lower levels of adversity. Elevated adversity, encompassing events like maltreatment, disregard, or discord in the home, is linked to deficiencies in multiple cognitive areas, such as executive functioning, memory, focus, and linguistic proficiency.

Conversely, those who have encountered less adversity, typically exhibit better cognitive outcomes. Although the precise processes underlying these correlations are varied, factors such as stress, disturbed neurodevelopment, and environmental influences, all work together to influence cognitive development. Secondly, at a cognitive and neuronal level, it appears that early adversity influences cognitive reserve later in life. According to a study by Teicher et al. (2016), childhood maltreatment, maybe linked to aberrant structural connectivity

in the cerebral cortex. In their review, the authors found that child brain development trajectories are altered by child maltreatment, which further appears to other neuronal circuitry such as the sensory system, and circuits responsible for emotional regulation, threat detection, and reward systems (Teicher et al., 2016). As such, early childhood developmental malformations may be the foundation of deficits observed in memory, attention, executive function, and emotional control dysregulation. These findings echo those by Moriguchi and Shinohara (2018), which indicate that childhood adversity alters structural prefrontal function, associated with diminished emotional processing and cognitive control observed in low SES samples (Moriguchi & Shinohara, 2018).

Further to the above, stress resulting from childhood adversity has been indicated to dysregulate the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, by raising cortisol levels and prolonging the activation of stress response systems (Moriguchi & Shinohara, 2018). The prolonged elongation of stress response systems is thought to lead to disruptions to synaptic plasticity and neuronal function, which impede cognitive development (Moriguchi & Shinohara, 2018).

As previously stated, the effects of ACEs on cognition and cortical function may persist into adulthood (Kobayashi et al., 2020). The persistence contributes to increased mental health problems including anxiety, depression, and post-traumatic stress disorder (PTSD) (Steptoe et al., 2019). At a cognitive level, it is thus plausible that early-life stressors, and adverse childhood experiences may affect cognitive performance, by dysregulating intricate neurobiological processes, the underly brain development and mental health outcomes (Webster, 2022).

In response to answering my first research question which investigated whether attention outcomes amongst children living with HIV are mediated by the experience of greater (four or more), or fewer experiences of ACEs (three or less), the converging findings seem to

indicate that higher experiences of ACEs, may be associated with poorer outcomes in attention scores.

5.1.2. ACE, Sex and HIV Neurocognition

Research Question Two

There is limited knowledge of the effect of sex and adversity on cognitive outcomes. With regard to the effect of sex, adversity, and HIV, findings indicated that females performed better than male participants on multiple attention measures, besides females experiencing a higher number of child adversities (47.6%) compared to males (40%). Explanation of this study findings can be reasoned by the work by Heim et al. (2008). The authors investigated the relationship between experiences of early life stressors, and depression, on cognition. Findings indicated that females who experienced early adversity such as emotional abuse, had decreased levels of oxytocin, which has been linked to cognitive decline (Heim et al., 2008). Furthermore, early experiences of stress, anxiety, and post-traumatic stress disorder (PTSD), have been found to adversely affect HIV positive female cognitive function.

In addition to the above, studies indicate that variances in cognitive ability may be influenced by biological differences between males and girls, including differences in the structure and function of the brain, hormonal impacts, and genetic predispositions (Cahill, 2006). For example, different cognitive strengths and limitations may arise from differences in brain organisation and connection patterns between sex (Ingalhalikar et al., 2014). sex -specific variations in hormone levels, especially those of oestrogen and testosterone, can also have an impact on cognitive functions as memory and spatial awareness (Cahill, 2006).

Conversely, socialization practices and cultural norms play a significant role in shaping sex differences in cognitive performance. From early childhood, boys and girls are socialized differently and exposed to varying expectations and opportunities based on sex stereotypes (Halpern et al., 2007). These societal influences can impact self-perception, academic interests,

and approaches to learning, ultimately influencing cognitive development and performance (Halpern et al., 2007).

Moreover, with reference to females, research indicates that females, on average, perform better than males on cognitive tasks that require sustained attention (Balart and Oosterveen, 2019). Furthermore, Walsh et al.(2019 argue that, in general, females outperform males on most neurocognitive tasks, except for visuospatial tasks. Therefore, such findings may indicate why females performed better than males.

Moreover, beside the above cited findings, females who experienced greater levels of ACEs, in my study, performed better than males who experienced less ACEs. These findings can be explained by resilience, a key variable in adversity studies. According to Woollett et al. (2016), resilience has the potential to enhance both physical health and cognitive outcomes. Since children and adolescents living with HIV face multiple challenges such as stigma and post traumatic stresses, it has been hypothesised that children living with HIV, have developed resilience (Woollett et al., 2016) .Woollett et al. (2016), particularly note that children living with HIV, have developed relevant sets of beliefs, such as a belief in fate and an understanding of their strength and limitation in overcoming the adversity of living with HIV. It has thus been hypothesised that adversity develops character and imbues affected children with the ability to think critically about themselves, which in turn raises, self-worth, and proactive responsibility (Khangamwa et al., 2020).

According to Merchant et al. (2022) greater resilience has been associated with improved cognitive functioning, encompassing executive, memory, and attentional domains. Higher resilience levels may be associated with better cognitive function. Furthermore, age-related cognitive decline may be warded off by resilience. That is, High levels of resilience have been associated with maintaining cognitive abilities and reducing the risk of cognitive impairment (Merchant et al., 2022).

In addition to the above, Yang and Wang, (2022) noted that in educational settings, resilience is linked to positive outcomes. Resilient students may demonstrate improved learning capacities, better cognitive flexibility, and greater academic achievement, in the face of diverse learning problems (Liu & Boyatzis, 2021; Yang & Wang, 2022). With further reference to females, studies on sex and resilience have hypothesised that females may be more resilient than men when faced with difficult situations. This resilience may be linked to interpersonal abilities, adaptive coping strategies, and social and emotional support. Furthermore, better performance in females can be explained heightened cognitive reserve (Lövdén et al., 2020). According to Friese and Yang, (2022) cognitive reserve, has an influence on educational and mental health outcomes. Accordingly, high cognitive reserve observed in females, indicates this population may be better able to withstand detrimental childhood effects, such as trauma, which may otherwise have an inadvertent effect on males. (Friese & Yang, 2019).

Notwithstanding, better outcomes in females on cognition, Ene (2018) investigated the relationship between HIV diagnosis, sex and cognition in young participants. Findings indicated that males living with HIV performed better on working memory tasks, compared to females of the same status (Ene, 2018). Noteworthy, findings from my study differ from those reported in Santoro et al. (2021). The authors found insignificant differences on cognitive outcomes, by sex, amongst children who experienced high and low childhood adversity, while my study predicted poorer cognitive outcomes amongst male participants. Significantly, findings from Santoro et al. (2021), are similar to those reported by Nooner et al. (2017), who report insignificant cognitive outcomes, between males and females who have experienced ACEs on multiple neuropsychological assessments on the Wechsler Intelligence Scale for Children.

Overall, converging evidence with reference to sex, ACEs, and HIV neurocognitive outcomes seems to suggest lack of clarity on the role of childhood adversity on sex. (Nooner et al., 2017). To succinctly summarise the second research investigation the study found a significant difference in attention outcomes between males and females when comparing high versus low adversity levels. Meaning that males performed poorly in attention tasks, when compared to females. Despite the potential influence of adversity on cognitive functioning, sex did not emerge as a significant factor affecting attention outcomes in the reviewed studies.

In response to the second research question which sought to investigate on whether attention outcomes amongst children living with HIV are influenced by biological sex and adversity experienced. The converging findings seem to suggest that other variables beyond sex may play a more prominent role in shaping attentional abilities in individuals exposed to varying levels of adversity.

5.1.3. ACE, Level of Education and HIV Neurocognition

Research Question Three

The third research question investigated the effect of education (High and Primary Schooling), ACEs (High vs Low), and attention outcomes. Contrary to the above literature, findings indicated that older high school students, suggested poorer attention outcomes, compared to primary school participants on the NEPSY. These findings are consistent with the data collected regarding the children's type of school they attend, academic performance, and grade repetition. The results may be indicative of the complex interplay between educational level and attention difficulties, suggesting that older students, despite having more advanced academic training, may experience increased stress and cumulative effects of ACEs that negatively impact their attention and cognitive functioning. To this end, demographic data indicated that 57% of participants, failed one or more school grades (See Appendix J) and that 24% of the children were either placed in special/remedial schools or, technical schools, due

to their inability to cope with the mainstream schooling. A proportion of the sample further reported experiencing significant learning difficulties.

The above findings are however, supported by findings from Zinyemba et al. (2019), who state that children living with HIV, may perform suboptimal, due to either falling ill, being orphaned, or due to financial constraints. Equally related to my findings, Qu et al. (2024), found that children with one or more ACEs, were 1.36 times more likely to repeat a grade, compared to those who have not experienced ACEs. Although Qu et al. (2024)'s findings were not based on children living in HIV care homes, their results suggest that ACEs have a significant effect on children and adolescents' education.

For example, Boyede et al. (2013) found that as children got older, they had poorer cognitive outcomes. Kaylee et al. (2021) investigated the cognitive performance of children aged 7-9 years (age-appropriate school grade) and are living with HIV. In their observational longitudinal study, they used a range of paediatric neuropsychological assessment including the Purdue Pegboard Test (PPT), which measure fine motor coordination (Klein, 2020), the Beery-Buktenika Development Test of Visual-Motor Integration (Beery-VMI), assessment measures visual perception and motor-coordination integration ability (Pfeiffer et al., 2015). Another assessment that was used was category fluency, which measured verbal generativity (Shao et al., 2014). Tshao and colleagues found that while the neurocognitive developmental trajectories of the treatment groups and controls showed significant similarities (i.e., performance improvements from 7 to 9), all children receiving ART, irrespective of the treatment arm, continue to be vulnerable to cognitive deficiencies beyond the early school age range (Kaylee et al., 2021).

Although no directional hypothesis was predicted, it was reasoned that younger participants (Primary education), who experienced a high number of ACEs, would perform less optimally than their high school counterparts, with either low or high ACEs. Pertaining to

educational level, Adverse Childhood Experiences (ACEs), and HIV neurocognition, the literature suggests that younger participants with primary education, who experienced a high number of ACEs, would perform worse in neurocognitive tasks compared to those with lower ACE exposure and higher educational attainment (McLaren et al., 2020). This pattern may reflect the compounding effects of early adversity and limited educational opportunities on cognitive development during critical periods of brain maturation. According to Lawson et al. (2017), maltreated children are more likely to be referred for special education services by the time they are in early primary school. Reduced grades, lower results on standardised assessments, and other measures of academic achievement are linked to a history of mistreatment. The dropout rate among general population is three times higher than that of maltreated children (Lawson et al., 2017). These findings are indisputable and cannot be explained by the impacts of other psychosocial stressors like poverty. They have been established across a variety of trauma exposures (e.g., physical abuse, sexual abuse, neglect, exposure to domestic violence (Lawson et al., 2017).

Kabuba et al. (2018) evaluated the impact of age and education amongst individuals living with HIV-1 clade C in Zambia on multiple neurocognitive functions including attention, learning, executive functions, and fine motor skills (Kabuba et al., 2018). Findings indicated younger participants (20-30 years) with greater cognitive reserve (indicated by greater school performance), outperformed less cognitively able individuals on neuropsychological assessment.

The above findings are supported by a systematic review by Musindo et al. (2018) which indicated that children (8-12) and adolescents (13-15) years had deficiencies in learning, simultaneous and sequential processing, and sequential processing. Importantly, the review indicated that neurocognitive deficiencies were related to socioeconomic adversity, and lower socioeconomic income, with primary school-aged children demonstrating pronounced

difficulties in attention, memory, and executive function compared to their high school counterparts.

The findings of this study could be further explained by the role of cortex in educational development. Bunge and Wright, (2007) argues that as children progress through different stages of development, the cortex undergoes structural and functional changes that support increasingly sophisticated cognitive functions. For example, the prefrontal cortex, involved in executive functions such as planning, decision-making, and self-regulation, undergoes significant development during adolescence, contributing to improved cognitive control and higher-order thinking skills (Crone & Dahl, 2012).

While it is expected that younger children may be characterised by shorter attention spans, greater distractibility, and older children exhibit improvement in attentional control, selective attention, and the ability to inhibit distractions may emerge, reflecting the maturation of neural circuits supporting attentional processes (Rueda et al., 2004),factors such as temperament, cognitive abilities, socio-economic status, and early-life experiences can all influence attentional development (Diamond, 2013).Previously reviewed studies regarding attention further corroborate these findings as they have indicated that attention, modulated by norepinephrine, may be disrupted in HIV infection as time progresses (Wang et al., 2017). .

Although limited, converging seems to suggest that as children grow older there is improvement in attentional control and the ability to inhibit distractions (Rueda et al., 2004). Younger participants in primary school tend to perform better than those in high school due to being less exposed to ACEs, and receiving early ART. Following the third research question which sought to investigate whether the level of education has an impact on attention outcomes of children living with HIV and who have experienced childhood adversity, the findings propose that a high number of adversities predicts poorer educational outcomes, and due to various factors, such as HIV affecting the neurocognition, poorer attention outcomes may be

expected as the child grows older. These findings are further supported by the educational context of the children.

5.1.4. ACE, Age and HIV Neurocognition

Research Question Four

In the last investigation, I sought to study whether there were significant differences in attention outcomes by age (young children: ages 10-13 years; and older children: ages 14-16 years), based on adversity (Low vs High)? Cognitive function continues to develop by brain maturation ((DelGiudice, 2017; Rice et al., 2014) with attention, developing exponentially, from infancy to middle childhood (Milligan & Cockcroft, 2017), with older participants (12 - 16 years) displaying greater mastery of working memory and attention skills. Findings from this study, indicated that, contrary to expectation, younger participants (10-13 years of age), performed better on the Auditory Attention Omissions Total Errors, and Response Set Omission attention subtests compared to older participants (>14 years). These findings were similar to those of Debeaudrap et al. (2018) and Weber et al (2017).

Debeaudrap et al. (2018) evaluated the effect of early prenatal HIV treatment on school-age neurodevelopmental outcomes among children living in Cameroonian, aged between 4 and 9 years of age. Findings from the KABC-II indicated that children receiving early ARVs, performed similarly to their HIV-negative counterparts of the same age (Debeaudrap et al., 2018). While Weber et al. (2017), illustrated that early intake of CART was linked with lower plasma viral loads, and similar cognitive performance to uninfected participants on the Wechsler Intelligence Score for Children, (WISC-IV). The results of my study may be indicative that early initiation of ARV treatment in children, maybe associated with favourable cognitive outcomes.

Findings from this study further revealed that elderly children (14-16 years), with higher ACEs, performed poorly on the cognitive domain of attention and concentration. These

findings are supported by Sheridan and McLaughlin, (2016), who found that in their study, a higher number of ACEs, associated with chronic stress, leads to difficulties, associated with concentration, memory, and executive functions, in children and adolescents aged 6 to 18 years.

Notwithstanding the above, older participants (14-16 years), regardless of ACE status, (High, or Low), performed better on attention measures. These findings are similar to those reported by Ardila et al. (2000) who demonstrated that performance on neuropsychological tests was significantly influenced by age and years of education (Ardila et al., 2000). Most importantly, older participants performed better in verbal fluency subtests, and this was attributed to their educational levels and that verbal fluency assessments required greater intelligence quotients (IQ), which is improved by age (Lehtinen et al., 2023).

With reference to the South African context, findings from my study are, however, dissimilar to those by Santoro et al. (2021) who found insignificant differences in cognition outcomes, by age, and adversity (High vs Low) within an HIV sample. In their study Santoro et al. (2021), found that both groups (High / Low), performed poorly on processing speed, and executive functions irrespective of age and adversity (Santoro et al., 2021).

There appears to be inconclusive evidence regarding the relationship between younger (10-13) and older (14-16) children who have experienced adversity. With younger participants performing better in some attention tasks, and older participants perform better on others. According to a meta-analysis conducted by Smith and Karaman (2019), the findings suggest that while younger participants may perform better in some attention tasks, older participants may excel in others. This variability in performance across different tasks underscores the complexity of assessing the impact of adversity on cognitive functioning across age groups (Smith and Karaman, 2019). The lack of clear differentiation between the groups may be due to several factors, including the heterogeneity of adverse experiences, individual differences in

coping mechanisms, and the presence of protective factors within the child's environment (Smith and Karaman, 2019).

Furthermore, developmental trajectories and the timing of exposure to adversity may also contribute to the inconsistent findings observed in research studies. For instance, children who experience adversity at a younger age may demonstrate different cognitive outcomes compared to those who experience adversity during adolescence (Hambrick et al., 2019). Therefore, when considering the age difference between the younger and older participants, there is no clear differentiation to make a conclusive comparison based on age.

Additionally, methodological limitations such as small sample sizes may further obscure the understanding of this relationship. For instance, the limitation in this study with reference to age was that the age band was too narrow to make inferential differences as the growth spurts were too similar. Conversely, the findings of the study could be explained in terms of the theory of stages of development proposed by Jean Piaget. Piaget's Cognitive Development, theory provides insights into why there may not be a clear differentiation between groups to make conclusive comparisons based on age. According to Piaget (1971), children progress through distinct stages of cognitive development, characterized by qualitatively different ways of thinking and understanding the world.

According to Piaget's developmental theory (1971), a person's cognitive development is impacted by their own experiences, maturity, and contextual circumstances in addition to their chronological age. It is therefore difficult to make firm conclusions based only on age because children in the same age group may exhibit heterogeneity in their cognitive capacities and problem-solving techniques. Accordingly, Piaget (1971), suggested that infants actively create their conception of the world through interactions with their surroundings, utilising assimilation, and accommodation processes to modify their preexisting mental schemas in response to novel knowledge and experiences. This dynamic process of cognitive development

may cause inconsistent performance on various tasks and performance swings, especially while developmental stages are changing (Piaget, 1971). In replying to the fourth research question on whether age has an effect on attention outcomes, in children living with HIV, who equally experienced high ACEs, findings suggest that suggest that cognitive capacities grow nonlinearly and are impacted by a wide range of variables other than age.

5.2. Limitations and Suggestions for Future Research

5.2.1. Methodological Considerations Affecting Findings

Quantitative Approach

Although the present study took the quantitative approach to answer the research questions under investigation, the study could have benefited from a mixed methods approach. Significantly, this approach enables a more comprehensive and nuanced examination of the research topic, facilitating for a thorough investigation of the topic under discussion. To this end, qualitative investigations could have enabled me to better explore the different *types* of *adversity* children may have experienced, and this would have enabled a nuanced investigation of the role of adversity, and resilience on HIV neurocognition outcomes.

Additionally, the mixed method approach would have enabled the investigation of childhood experiences, what (if any), child coping strategies, and what (if at all), personality traits, mitigated child adversity, and influenced cognitive function outcomes. To this end, research indicates that personality traits influence cognition and that extraversion and neuroticism, are linked to individuals indicating higher or lower attentional control. Further exploration of factors such as personality and resilience may have added to the study findings (Hu et al., 2022).

Moreover, qualitative interviews could have helped mitigate reporting bias, due to either participants, or guardians, omitting or overreporting, information on the ACEs

Questionnaire. It is thus recommended that future studies develop on the current findings by implementing a mixed method approach to the study on adversity in adolescent HIV.

Instrumental Validity

In addition to the above limitation, my study, used The Paediatric Adverse Childhood Experiences Questionnaires, which, although found to have high face validity (Koita, et al. 2018), lacks content validity, for the South African context. For example, items within the scale, required participants, to know or recall, household members who were depressed, mentally ill or attempted to commit suicide. Such topics, although indicative of childhood adversity, tend to be taboo, in certain African context (Monnapula-Mazabane & Petersen, 2023) and their inclusion, may be an invalid measure of early childhood adversity in my study context. Given the above, the study could have benefitted from using culturally appropriate assessment instruments that take into account a more comprehensive picture of childhood adversity in the South African setting, and using validated instruments created or modified especially for groups with different cultural origins could be one way to achieve this (Foxcroft & Roodt, 2012). The validity and applicability of the study's conclusions may also be increased by using qualitative techniques like focus groups or interviews, which can provide deeper insights into culturally sensitive accounts of childhood adversity (Gill & Baillie, 2018).

5.2.2. Sample Size

Lastly, my study was plagued by a small sample size. The current study was limited to collecting data from two HIV shelters, resulting in a limited sample size, for inferential analysis. It is recommended that future studies could benefit from a larger sample size, evenly distributed by age, sex, ethnicity, and level of education.

5.3. Recommendations for Future Research

5.3.1. Neuroimaging

In addition to implementing mixed methods approaches, and increasing the sample size of the study, it is suggested that future studies could benefit from incorporating neuroimaging techniques, to the investigation of child adversity (High vs Low), to study HIV neurocognition. Leijser et al. (2018) investigated the neuroscience of socio-economic status (SES) and found that variations in SES are associated with differences in brain structure, function, and connectivity across the lifespan.

Similar Moriguchi and Shinohara (2019) who investigated socioeconomic dependent disparity in brain development, future studies could develop from using portable neuroimaging techniques such as functional near infrared spectrometry (fNIRS) imaging, to investigate study, cortical hypoactivation, or hyperactivation in relation to child adversity. fNIRS, neuroimaging, would for example, allow for the investigation of changes in oxygenated and deoxygenated haemoglobin concentrations, in response to task-based investigations, such as attention, and working memory, paired by childhood adversities determinants.

5.4. Significance of Study

Beside the limitations identified above; the current study contributes to the growing body of research investigating the impact of ACEs on HIV neurocognition. Significantly, the study expands on the seminal work of Santoro et al. (2021), by investigating the effects of ACEs, on a single cognitive domain and by introducing valid scales to study child adversity in the context of HIV. To this end, South Africa continues to have one of the highest rates of HIV, with a sizable proportion of its youth, affected infected by the virus. The execution of this thesis thus paves the way to investigating the cojoined effects of HIV in on cognition, with the promise of using this information to develop interventions protocols for affected children. Moreover, considering the unique sociocultural context of South Africa, characterised by historical difficulties, socioeconomic inequality, and a high incidence of ACEs, this type of research is timely. The study has highlighted the prevalence of ACEs in HIV care shelters

within South Africa, thus highlighting the importance of developing, specialised support services, and educational initiatives for children in these care shelters.

By highlighting the impact of ACEs, stakeholders can design comprehensive support services that not only address immediate needs but also foster long-term resilience and well-being among children affected by HIV. Additionally, educational initiatives targeted at children may empower children with knowledge and skills to navigate varied aspects of adversity they may have encountered. Ultimately, these efforts aim to improve the overall quality of care and support provided to vulnerable populations in HIV care shelters, leading to better outcomes for children and their families.

5.5. Reflexivity

Lastly, at this juncture, it is worth considering my positionality within the execution of the study. According to Alvesson and Sköldberg, (2018), reflective research consists of two characteristics, careful *interpretation* and *reflection*. Conducting research with children living with HIV/AIDS, was both a challenge and exhilarating experience. The experience of conducting research with vulnerable children, taught me patience, however, the experience filled with mixed emotions, particularly how to divorce my feelings as a researcher, with the compassion I had for the research participants. A key case in point was the challenge of not being able to adequately balance empathy and objectivity when interacting with children who shared their personal experiences of adversity. Despite feeling deeply for their adversities, maintaining a neutral stance was crucial to ensure the integrity of the research process and minimize potential bias.

Another example is the importance of establishing trust and rapport with the participants, especially considering the sensitive nature of the topics discussed. Furthermore, building a supportive and non-judgmental environment allowed the children to feel comfortable sharing their stories authentically, enhancing the quality and depth of the data

collected. Secondly, it was important to maintain an open and flexible frame of mind when children lacked the zeal to perform at their best. The lack of performance affected me as a researcher, but I needed to control it by refraining from imposing unrealistic expectations on the children. Instead, I adjusted my approach by providing additional encouragement and support tailored to their individual needs and circumstances. For example, acknowledging their efforts and highlighting their strengths helped foster a positive environment conducive to participation.

Moreover, I was able to identify the different elements—such as exhaustion, worry, or environmental distractions that can affect the performance of children by exercising patience and empathy. By remaining empathetic and adaptable, I adapted the research protocols as needed to accommodate the children's comfort and engagement levels. For instance, offering breaks or incorporating interactive activities helped alleviate tension and reinvigorate their interest in the research tasks.

Additionally, maintaining a non-judgmental attitude and demonstrating genuine interest in their perspectives encouraged open communication and mutual respect between myself and the participants. Creating a safe space where children felt valued and heard empowered them to express themselves authentically, even if their performance varied at times. Ultimately, prioritizing the well-being and dignity of the children while upholding the integrity of the research process was paramount in navigating challenges and fostering meaningful connections throughout the research endeavour.

In line with this, I acknowledged that my use of gestures may have affected the objectivity of data collection. As a researcher working with children, their lack of performance could certainly affect me, especially if I had high expectations for their engagement or if I felt pressure to collect quality data. However, this was mitigated by implementing standardised protocols and implementing the assessment practitioner's duties during the data collection. As

a psychometrist I needed to ensure consistency in gesture interpretation across different participants. For instance, argue that individuals with negative past experiences may have developed a negative attitude towards undergoing an assessment, and as an assessor, it was important to be considerate and sensitive towards their experiences and behaviour.

I controlled my reactions by reminding myself of the variability in children's abilities and considering factors such as fatigue, distractions, or discomfort that might impact their performance. Additionally, I focused on creating a supportive and non-judgmental environment that encouraged children to participate at their own pace, thereby reducing the pressure on both them and me. Other social contexts such as race and social class can profoundly influence data collection processes, shaping both researcher-participant dynamics and the interpretation of findings. Research indicates that researchers'' own racial and social class backgrounds can inadvertently introduce biases and affect their interactions with participants (Smedley et al., 2003). Furthermore, participants'' perceptions of the researcher's race and social class can impact their trust and willingness to disclose information, potentially skewing the data collected (Karbeah & Hacker, 2023).

Systemic inequalities linked to race and social class also impact access to research opportunities, leading to underrepresentation and exclusion of marginalised groups (Dovidio et al., 2016). My sample was mainly populated by black children; however, I was not oblivious to the marginalised groups that were part of the sample. Therefore, to mitigate bias and ensure diverse groups are represented in this study, it was important to reflect on the sampling strategies and methodologies of the study. Though the sample was inclusive in nature, a larger sample would have helped further mitigate racial bias.

Lastly, my positionality as a female, conversant in multiple languages, may have enabled me to solicit and create a positive rapport and research environment, which I believe resulted in quality data being sourced from participants. Moreover, my roles as a female may

have contributed to my ability to relate to participants'' experiences in complex ways, leading to greater comprehension. The fact that the participant was female may also have encouraged her to feel more comfortable sharing private material, which would have added a variety of viewpoints and anecdotes to the research findings.

CHAPTER 6: CONCLUSIONS

HIV significantly impacts children's cognitive development, extending beyond acute clinical effects. Research highlights multiple mechanisms through which HIV affects neurocognition, including direct effects on the central nervous system and potential adverse effects from antiretroviral drugs. HIV's effect on the CNS, leads to disruption, in cognitive outcomes, especially attention, and school experiences, potentially causing delays in cognitive milestones and academic achievements. Moreover, the effect of HIV, on cognition is compounded by adverse childhood experiences.

The current study underscores the compounded effect of ACEs on neurocognition, in relation to living with HIV. This study is the first to investigate the relationship between ACEs, and attention skills, especially in children living with HIV, placed in HIV care shelters. Cumulatively, findings seems to indicate that higher ACEs (> 4), are associated with poorer cognitive outcomes, in attention and executive functions. . Although moderators such as, timely initiation of ARVs, premorbid cognitive skills, age, and sex, are key consideration and determinants in cognitive outcomes, childhood adversity appears to be a considerable predictor of cognitive skills in HIV.

While inconclusive, age, level of education, and biological sex, provide nuanced capacities in shaping neurocognitive outcomes, however, findings suggest that resilience may emerge as a potential protective factor, in determining cognitive outcomes, within a sample of children living with HIV, in care shelters. To enhance study findings, larger samples, and the implementation of robust experimental designs, incorporating neuroimaging technology, may extend knowledge pertaining to the intertwined nature of ACE prevalence, HIV, and neurocognition. In conclusion, investigating the relationship between Adverse Childhood Experiences (ACEs) and attention skills in children living with HIV has revealed that ACEs significantly worsen cognitive and attentional difficulties in this population. Children with HIV

who have experienced trauma, neglect, or other adverse events exhibit greater challenges in attention and executive functioning compared to those with fewer or no ACEs. The compounded effects of chronic health conditions and early adversities contribute to heightened risks of cognitive impairments and attentional deficits. This underscores the importance of early intervention and support systems tailored to address both the medical and psychological needs of these children, to mitigate the adverse impact of ACEs on their cognitive development and overall well-being.

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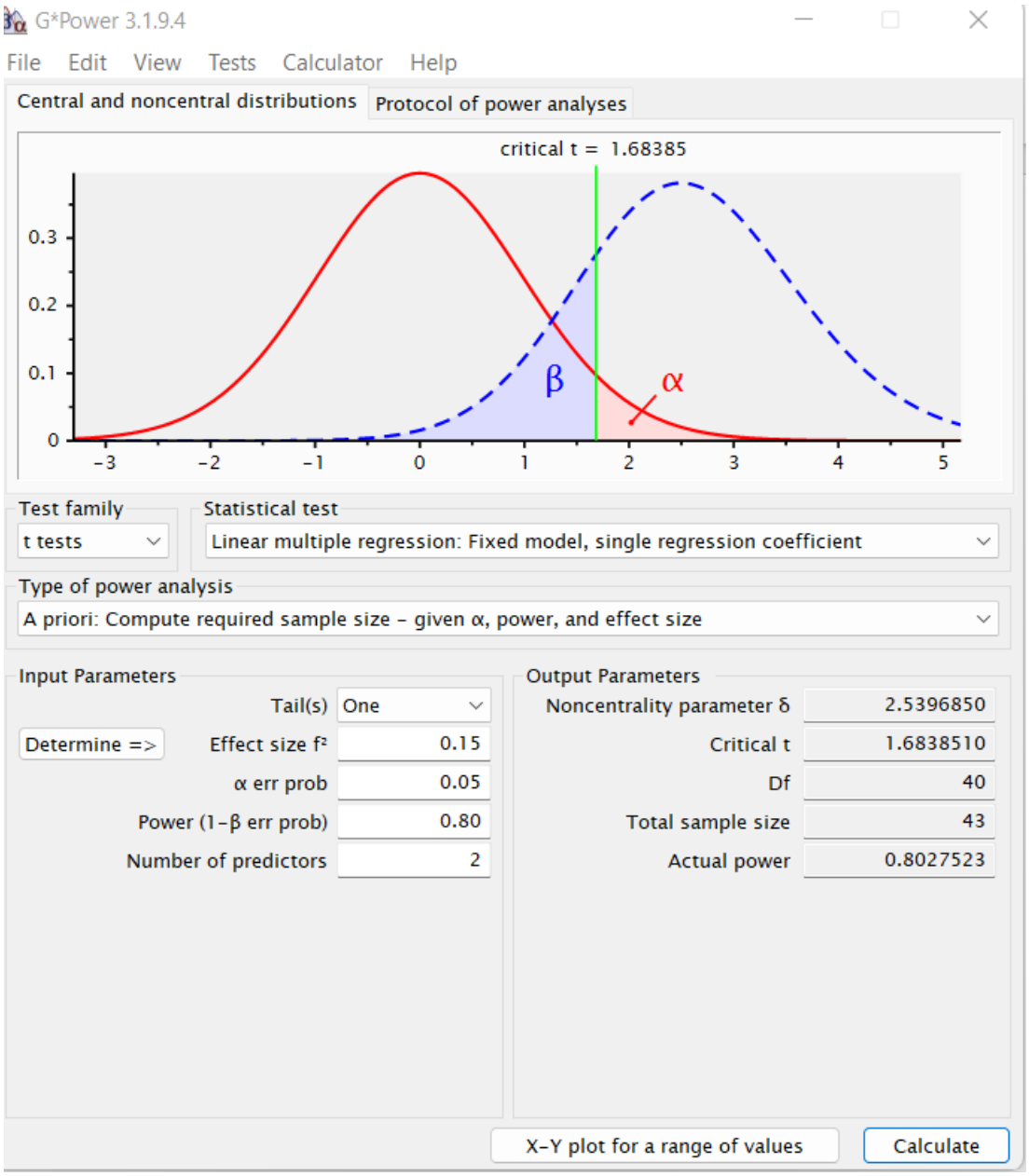
APPENDICES

APPENDIX A



Note: The G*power 3.1.9.4 software was used to compute the effect size of the required sample to conduct the study. A linear multiple regression statistical test was run in order to obtain the estimate of the sample size.

APPENDIX B

Administered Demographic Questionnaire

Psychology
School of Human & Community Development
University of the Witwatersrand
Private Bag 3, Wits, 2050
Tel: 011 717 4503
Fax: 011 717 4559

Your name:	Date:
Childs Name:	School:
Age of Child:	Date of Birth
Name of Shelter	

1. Childs Sex: (circle one):	**Male**	**Female**	
2. Childs 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 30 minutes?

Yes ☐ No ☐

If Yes please specify_____

(c) **Psychiatric disorders**: Has your child shown any pattern of behaviour 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 C

CYW Adverse Childhood Experiences Questionnaire Teen (ACE-Q) Teen

To be completed by Parent/Caregiver

Today's Date: _____

Child's Name: _____ Date of birth: _____

Your Name: _____ Relationship to Child: _____

Many children experience stressful life events that can affect their health and wellbeing. The results from this questionnaire will assist your child's doctor in assessing their health and determining guidance. Please read the statements below. Count the number of statements that apply to your child and write the total number on the line provided.

Please DO NOT mark or indicate which specific statements apply to your child.

1) Of the statements in Section 1, HOW MANY apply to your child? Write the total number in the box. ☐

Section 1. *At any point since your child was born…*

- Your child's parents or guardians were separated or divorced
- Your child lived with a household member who served time in jail or prison
- Your child lived with a household member who was depressed, mentally ill or attempted suicide
- Your child saw or heard household members hurt or threaten to hurt each other
- A household member swore at, insulted, humiliated, or put down your child in a way that scared your child OR a household member acted in a way that made your child afraid that s/he might be physically hurt
- Someone touched your child's private parts or asked them to touch that person's private parts in a sexual way that was unwanted, against your child's will, or made your child feel uncomfortable
- More than once, your child went without food, clothing, a place to live, or had no one to protect her/him
- Someone pushed, grabbed, slapped or threw something at your child OR your child was hit so hard that your child was injured or had marks
- Your child lived with someone who had a problem with drinking or using drugs
- Your child often felt unsupported, unloved and/or unprotected

2) Of the statements in Section 2, HOW MANY apply to your child? Write the total number in the box. ☐

Section 2. *At any point since your child was born…*

- Your child was in foster care
- Your child experienced harassment or bullying at school
- Your child lived with a parent or guardian who died
- Your child was separated from her/him primary caregiver through deportation or immigration
- Your child had a serious medical procedure or life threatening illness
- Your child often saw or heard violence in the neighborhood or in her/his school neighborhood
- Your child was detained, arrested or incarcerated
- Your child was often treated badly because of race, sexual orientation, place of birth, disability or religion
- Your child experienced verbal or physical abuse or threats from a romantic partner (i.e. boyfriend or girlfriend)

CYW Adverse Childhood Experiences Questionnaire (ACE-Q) Teen Self-Report

To be completed by Patient

Today's Date: _____

Your Name: _____ Date of birth: _____

Many children experience stressful life events that can affect their health and development. The results from this questionnaire will assist your doctor in assessing your health and determining guidance. Please read the statements below. Count the number of statements that apply to you and write the total number in the box provided.

Please DO NOT mark or indicate which specific statements apply to you.

1) Of the statements in section 1, HOW MANY apply to you? Write the total number in the box. ☐

Section 1. *At any point since you were born...*

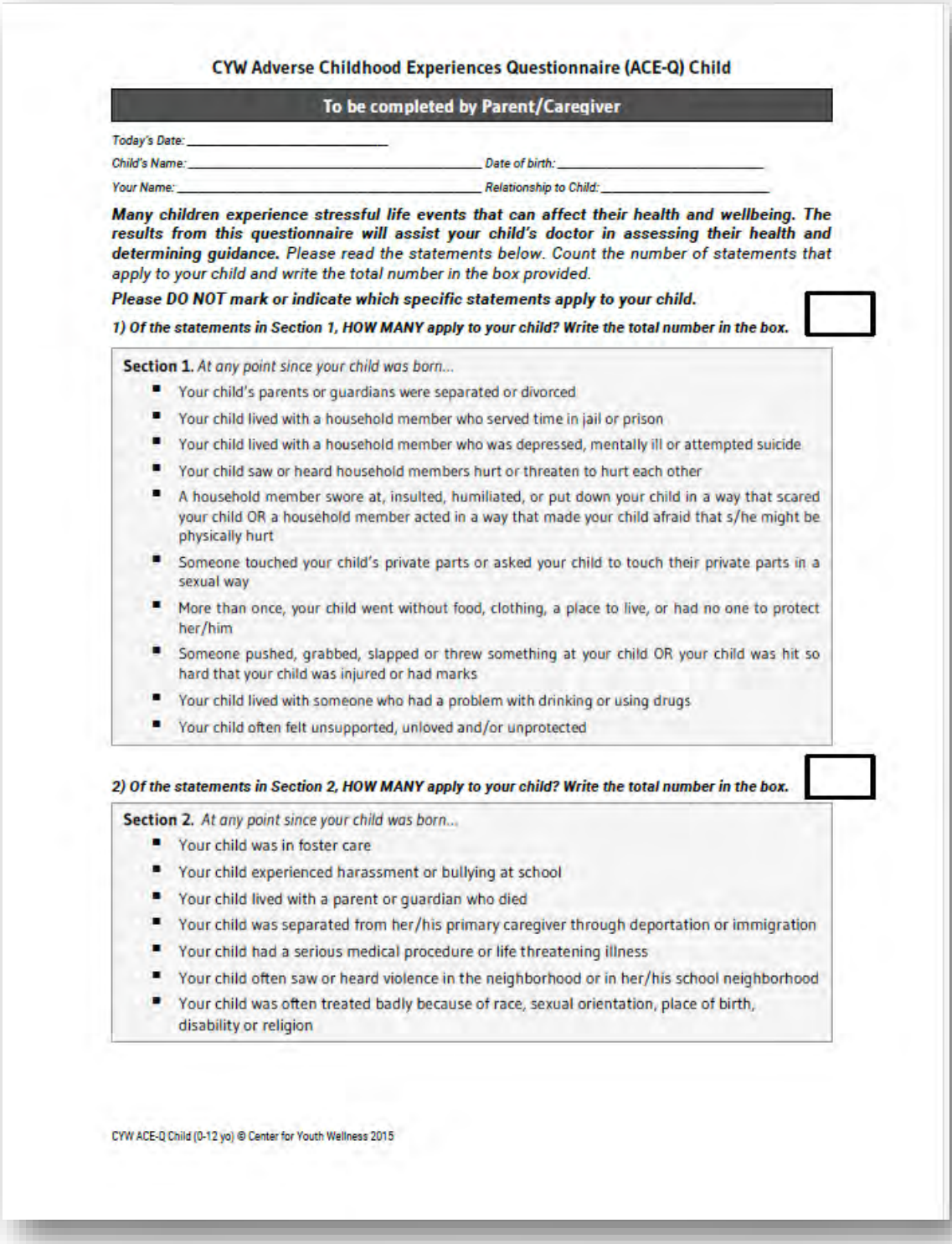
- Your parents or guardians were separated or divorced
- You lived with a household member who served time in jail or prison
- You lived with a household member who was depressed, mentally ill or attempted suicide
- You saw or heard household members hurt or threaten to hurt each other
- A household member swore at, insulted, humiliated, or put you down in a way that scared you OR a household member acted in a way that made you afraid that you might be physically hurt
- Someone touched your private parts or asked you to touch their private parts in a sexual way that was unwanted, against your will, or made you feel uncomfortable
- More than once, you went without food, clothing, a place to live, or had no one to protect you
- Someone pushed, grabbed, slapped or threw something at you OR you were hit so hard that you were injured or had marks
- You lived with someone who had a problem with drinking or using drugs
- You often felt unsupported, unloved and/or unprotected

2) Of the statements in section 2, HOW MANY apply to you? Write the total number in the box. ☐

Section 2. *At any point since you were born...*

- You have been in foster care
- You have experienced harassment or bullying at school
- You have lived with a parent or guardian who died
- You have been separated from your primary caregiver through deportation or immigration
- You have had a serious medical procedure or life threatening illness
- You have often seen or heard violence in the neighborhood or in your school neighborhood
- You have been detained, arrested or incarcerated
- You have often been treated badly because of race, sexual orientation, place of birth, disability or religion
- You have experienced verbal or physical abuse or threats from a romantic partner (i.e. boyfriend or girlfriend)

APPENDIX D



CYW Adverse Childhood Experiences Questionnaire (ACE-Q) Child

To be completed by Parent/Careqiver

Today's Date: _____

Child's Name: _____ *Date of birth:* _____

Your Name: _____ *Relationship to Child:* _____

Many children experience stressful life events that can affect their health and wellbeing. The results from this questionnaire will assist your child's doctor in assessing their health and determining guidance. *Please read the statements below. Count the number of statements that apply to your child and write the total number in the box provided.*

Please DO NOT mark or indicate which specific statements apply to your child.

1) Of the statements in Section 1, HOW MANY apply to your child? Write the total number in the box. ☐

Section 1. *At any point since your child was born...*

- Your child's parents or guardians were separated or divorced
- Your child lived with a household member who served time in jail or prison
- Your child lived with a household member who was depressed, mentally ill or attempted suicide
- Your child saw or heard household members hurt or threaten to hurt each other
- A household member swore at, insulted, humiliated, or put down your child in a way that scared your child OR a household member acted in a way that made your child afraid that s/he might be physically hurt
- Someone touched your child's private parts or asked your child to touch their private parts in a sexual way
- More than once, your child went without food, clothing, a place to live, or had no one to protect her/him
- Someone pushed, grabbed, slapped or threw something at your child OR your child was hit so hard that your child was injured or had marks
- Your child lived with someone who had a problem with drinking or using drugs
- Your child often felt unsupported, unloved and/or unprotected

2) Of the statements in Section 2, HOW MANY apply to your child? Write the total number in the box. ☐

Section 2. *At any point since your child was born...*

- Your child was in foster care
- Your child experienced harassment or bullying at school
- Your child lived with a parent or guardian who died
- Your child was separated from her/his primary caregiver through deportation or immigration
- Your child had a serious medical procedure or life threatening illness
- Your child often saw or heard violence in the neighborhood or in her/his school neighborhood
- Your child was often treated badly because of race, sexual orientation, place of birth, disability or religion

CYW ACE-Q Child (0-12 yo) © Center for Youth Wellness 2015

APPENDIX E

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Rhodes University Human Research Ethics Committee
PO Box 94, Makhanda, 6140, South Africa
t: +27 (0) 46 603 7727
f: +27 (0) 46 603 8822
e: ethics-committee@ru.ac.za
NHREC Registration number: RC-241114-045

https://www.ru.ac.za/researchgateway/ethics/

22 July 2022

sibongile ngomane

Email: g21n2858@campus.ru.ac.za g21n2858@campus.ru.ac.za

Review Reference: 2022-5149-6934

Dear sibongile ngomane

Title: Investigating the Relationship Between Adverse Childhood Experience and Attention Skills in Children living with HIV in a South Africa Setting

Researcher: sibongile ngomane

Supervisor(s): Mrs Sibongile Ngomane,

This letter confirms that the above research proposal has been reviewed and **APPROVED** by the Rhodes University Human Research Ethics Committee (RU-HREC). Your Approval number is: 2022-5149-6934

Approval has been granted for 1 year. An annual progress report will be required in order to renew approval for an additional period. You will receive an email notifying you when the annual report is due.

Please ensure that the ethical standards committee is notified should any substantive change(s) be made, for whatever reason, during the research process. This includes changes in investigators. Please also ensure that a brief report is submitted to the ethics committee on the completion of the research. The purpose of this report is to indicate whether the research was conducted successfully, if any aspects could not be completed, or if any problems arose that the ethical standards committee should be aware of. If a thesis or dissertation arising from this research is submitted to the library's electronic theses and dissertations (ETD) repository, please notify the committee of the date of submission and/or any reference or cataloguing number allocated.

Sincerely,

Janet Hayward

Dr Janet Hayward

Chair: Rhodes University Human Research Ethics Committee, RU-HREC

cc: Ethics Coordinator

APPENDIX F

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PARENTS AND GUARDIANS INFORMED CONSENT

Project Title: Investigating the Relationship Between Adverse Childhood Experiences and Attention Skills in Children living with HIV in a South Africa Setting

1. Sibongile Ngomane from the Department of Psychology, Rhodes University has requested my permission to allow my child/ward to participate in the above-mentioned research project. The nature and the purpose of the research project, and this informed consent declaration have been explained to me in a language that I understand.

I am aware that:

2. The purpose of the research project is to investigate the relationship between Adverse Childhood Experiences and Attention skills in children living with HIV and to see the impact of adverse childhood experiences in children living with HIV.
3. The study forms part of a larger project being conducted by Rhodes University and the University of the Witwatersrand. The primary research supervisor of the study is the Principal investigator (PI) of the study.
4. Ethical approval for this study has been granted by the University of the Witwatersrand (Ethics Number MED-21-04109) and the Rhodes University Ethics Committee.
5. By participating in this research project my child/ward will be contributing towards the Primary Investigator and researcher's understanding of brain plasticity and HIV and finding effective interventions to improve attention skills in children living with HIV.
6. The study will comprise four parts. Part I of the study will include: (I) The parent/guardian /director reading through this information sheet (15 minutes) and completing a questionnaire (20-25 minutes). Once Part 1 is complete, Part 2 will commence.

Part 2 of the study will involve (I) the researcher explaining the study to my child/ward (I 5-20 minutes); and (2) my child/ward will read and complete an informed assent form (15 mins). Once my child/ward has provided informed assent, they will complete a series of assessments spread over two days. Day One of the assessment will involve my child/ward: (I) completing a pencil and paper task about childhood experiences. Day Two will include my child: (I) completing non-computerized activities that assesses attention skills.

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This session will involve the child/ward responding to questions and using materials with his/her hands to build some items. This session will take about2-3 hours to complete. All protocols related to the study will be completed at the children's home where the child/ward resides.

7. My child's/ward's participation is entirely voluntary, should the child/ward wish to withdraw from participating in the study, the child/ward will be free to do so without any consequences.
8. It is the parent's/guardian's/ director's right to request that the child/ward is withdrawn from the research before, the research has finished, even if the researcher or any other appropriate person feels it is in the child's/ward's best interests, or if the child/ward does not follow instructions.
9. There are no known harmful risks associated with the use of the NEPSY II. The ACEs questionnaire is, however, a sensitive questionnaire, and should the child/ward feel a need to receive counseling post completion or during the administration of the questionnaire, psychological services will be made available at no cost to the parent/guardian/director, or even the child/ward. The NEPSY assesses one's cognitive abilities and analyses attentional skills and abilities. The ACE questionnaire accesses one's childhood experiences.
10. The COVID-19 pandemic continues to be a challenge in our country. The researcher will take protective measures, to stop the possible spread of the virus, such as (a) ensuring the wearing of masks and maintaining social distance during the research. If any of the researchers report signs of COVID, after interacting with the child/ward, the researchers will contact you directly to inform you. I may also contact the researcher or Principal investigator immediately if my child/ward experiences any signs and symptoms of the virus during the study, or after completing the research study.
11. The researcher intends to publish the research results in the form of publications and make them available to the academic community through journal and conference publications. The director of the children's home where my child/ward resides may request a copy of the research findings, however, confidentiality and anonymity of all records will be strictly maintained.

12. The parent/guardian/director will not receive written/verbal feedback regarding the results obtained during the study unless specifically requested in the form of a phone number or email address provided at the end of this document.

13. Any further questions that the parent/guardian/director might have concerning the research or participation will be answered by:

    Contact Details of the Principal Investigator
    Please contact Mr Sizwe Zondo (S.Zondo@ru.ac.za I 046 603 8503). Student Researcher: Ms Sibongile Ngomane (g21n2858@campus.ru. ac. za)
14. By signing this informed consent declaration, I am not waiving any legal claims, rights, or remedies that I or my child/ward may have.

I parent/guardian/director, ... have read the above information / confirm that the above information has been explained to me in a language that I understand, and I am aware of this document's contents. I have asked all questions that I wished to ask, and these have been answered to my satisfaction. I fully understand what is expected of my child/ward during the research. I have not been pressurised in any way to let my child/ward take part.

By signing below, I voluntarily agree that my child /ward..... (insert name of child/ward), who is .....years old, may participate in the above-mentioned research project.

Parent's/Guardian's/Director's Signature:.....
Date.....

APPENDIX G

STUDY INFORMATION SHEET AND ASSENT FOR MINORS

Study Title: Investigating the Relationship Between Adverse Childhood Experiences and Attention Skills in Children living with HIV in a South African Setting

Greetings,

Why am I here?

We are researchers at Wits University, and Rhodes University conducting a study to understand the impact of adverse childhood experiences on the attention skills of children living with HIV. This study forms part of a larger project which examines cognitive rehabilitation for a paediatric HIV population: The case of sustained attention.

The researcher's part of the study is to investigate the relationship between Adverse Childhood Experiences (ACEs) and attention skills in children living with HIV in a South African setting. The researcher would like to invite you to join this study. The Participation Information Sheet for Minors explains the details of the study.

Details of Study

Should you join the study, you will be asked to complete some tasks. These tasks include (1) completing some pen and paper exercises daily, which will take about 20-30 minutes to complete. The daily tasks are for evaluating how you behave in the home and educational settings. (2) completing exercises that include you responding to questions.

How long will the study be?

The NEPSY and Adverse Childhood Experience (ACE) questionnaire will be administered at different times. The NEPSY activities will be done before the intervention treatment (from the larger project) only once. The ACE questionnaire will also be done before the intervention only once. If the child/ward gets tired during the exercises, regular breaks will be taken.

Do my parents know about this?

This study's information has been given to parents(s) or guardian/director, and s/he has agreed that the child/ward participates in the study. Although they agree for the child/ward to participate in the study, the decision to be involved is also the child/ward.

What are the Risks of the study?

There are potential risks involved. This includes exposure of children to COVID19. Precautionary measures set out by the department of health will be strictly adhered to, to minimize the possible exposure of the virus to the child/ward.

no known harmful risks are associated with administering the NEPSY II The NEPSY assesses one's cognitive abilities and analyses your attentional skills and abilities. The ACEs test assesses childhood experiences. Due to the sensitivity of the ACEs instrument items, counselling and or other psychological services will be provided to participants. To ensure that you are comfortable and relaxed when completing these activities, we will ensure that there is minimal to no distraction in, and outside the room.

The COVID-19 virus continues to be a challenge in our country. The virus is spread when we cough and touch surfaces that may be infected with the virus. We will take protective measures to stop the possible spread of the virus, such as (a) ensuring the wearing of masks, (b) and maintaining social distance during the research. Several health and safety measures will be put into place to prevent the spread of the virus during the study. These measures will be reviewed by the Health and Safety Officer at Wits University. If any of the researchers report signs of COVID, after interacting with the child/ward, or parent/guardian/director, each party involved will be directly informed. Please also contact the researcher immediately if the child/ward experiences any sign of the virus after completing the research study.

What are the benefits of the study?

As a participant in this study, there may be no direct benefit; however, the information that the researchers gather from the study will contribute to the understanding of the value of neurocognition and attention skill exercises in children living with HIV.

What about confidentiality and anonymity?

All the information collected during the study will be kept confidential (private). Anonymity (the organisation's name child's/ward's name, and other identifying information) and confidentiality are a high priority to the researchers, and this will be always secured. All information collected during the study will be secured and password-protected by the researchers. The researcher will also never use the child/ward's name, the organisation's name, or parent/guardian/director, but will instead use a number-identifying system to distinguish each participant in the study.

What about withdrawal from this study?

The participant is free to withdraw from the study at any time, and this decision will not be held against any participant. This decision can be discussed with the parent/guardian/ director and researcher.

What else should I know about the study: Research Outputs

Findings from this study will be published and made available to the academic community through journal and conference publications. The director of the children's home where the child/ward resides may request a copy of the research findings, but this will not affect you as all data will be anonymous.

If the parent/guardian/director has questions?

For questions about the study, please contact the Supervisor Mr. Sizwe Zondo at 046 603 8503), or Ms. Sibongile Ngomane (g21n2858@campus.ru.ac.za)

AGREEMENT TO BE IN THE RESEARCH STUDY

The signature below means the child/ward has read the above information about the research study and t had a chance to ask questions to help understand what will be done during the study. This signature also means participants can withdraw from the study at any point they wish or want to.

Name of Participant: _____

Date _____

Place _____

Signature _____

APPENDIX H

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 Johannesburg Children's Home 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

14 December 2021
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX I

COVID-19 PROTOCOL FOR RESEARCHERS

Researchers should adhere to specific COVID-19 protocols to ensure their and participants' safety during research activities. These protocols typically include:

1. **Pre-screening and Health Checks**: Researchers should conduct pre-screening assessments for COVID-19 symptoms and exposure risks among themselves and participants before any in-person interactions.
2. **Personal Protective Equipment (PPE)**: Researchers should wear appropriate PPE, such as masks, gloves, and face shields, especially during face-to-face interactions or when working in close proximity to others.
3. **Physical Distancing**: Maintain a safe distance of at least 6 feet (2 meters) from participants and colleagues whenever possible. Arrange research settings to allow for adequate physical distancing.
4. **Hygiene Practices**: Encourage frequent handwashing with soap and water for at least 20 seconds or the use of hand sanitizer with at least 60% alcohol content. Ensure that research environments are equipped with hand hygiene facilities.
5. **Disinfection and Sanitization**: Regularly clean and disinfect high-touch surfaces and shared equipment in research settings. Provide disinfectant wipes or sprays for researchers and participants to clean surfaces as needed.
6. **Remote Data Collection**: Whenever feasible, consider conducting research activities remotely using virtual platforms to minimize face-to-face interactions and reduce transmission risks.
7. **Minimize Group Gatherings**: Limit the size of research groups or meetings to comply with local guidelines and regulations regarding gatherings and social distancing.
8. **Compliance with Local Regulations**: Stay informed about and comply with local, national, and institutional guidelines and regulations related to COVID-19 prevention measures and research activities.
9. **Flexibility and Adaptability**: Be prepared to adapt research protocols and procedures in response to changing COVID-19 conditions and guidelines to prioritize the health and safety of all involved.

APPENDIX J

EDUCATIONAL HISTORY OF CHILDREN LIVING WITH HIV AND ARE IN HIV CARE SHELTERS

Variables			
	Sample (N)	Females (%)	Males (%)
Primary School			
Mainstream School	8	63%	37%
Special /remedial school	0	0	0
High School			
Technical School	5	6%	9%
Mainstream School	24	29%	41%
Special/remedial School	5	9	6%
Grades repeated			
Grades repeated (once)	11	73	27%
Grades repeated (more than once)	12	25%	75%
Learning difficulties	14	43%	57%
ACEs			
High Aversity	31	68%	32%
Low Adversity	11	73%	27%