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McKillop, Brittany

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Working memory profiles of children with the Human Immunodeficiency Virus (HIV): A comparison with controls

Brittany McKillop

385493

Supervisor: Prof. Kate Cockcroft

Department of Psychology

A research report submitted to the Faculty of Humanities, University of the Witwatersrand, Johannesburg, in partial fulfillment for the degree of Masters of Arts in Psychology by Coursework and Research Report

Declaration

I hereby declare that this research report is my own independent work, and has not been presented for any other degree at any other academic institution, or published in any form.

It is submitted in partial fulfillment of the requirements for the degree of Masters of Arts in Psychology by Coursework ad Research Report at the University of the Witwatersrand, Johannesburg.

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Brittany McKillop May 2014

(385493)

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Abstract

With 10% of the population being infected with Human Immunodeficiency Virus (HIV), South Africa has the highest number of infections in the world (StatsSA, 2013). HIV results in cognitive and motor deficits in children as the severe compromise of the immune system leads to neurodevelopmental dysfunction peri-natally (Ruel, Boivin, Boal, Bangirana, Charlebois, & Havlir, 2011). Neurocognitive deficits affect overall general intellectual abilities and include difficulties with attention and speed of information processing, verbal language, executive –abstraction, complex-perceptual motor function, memory and motor and sensory function (Dawes & Grant, 2007). Developmentally, it is evident that working memory provides a crucial interface between perception, attention, memory and action (Baddeley, 1996; Baddeley 2003). Therefore the purpose of the study was to investigate the working memory profiles of both an HIV positive children and a control sample, on cognitive tasks (Automated Working Memory Assessment), general intellect tasks (Raven's Colored Progressive Matrices) and language competence tasks (Sentence Repetition Test). The current study compared 26 HIV positive children (mean age = 6.58 years) to 26 matched controls (mean age = 6.73 years).

It was found that both non-verbal IQ and language proficiency were correlated to HIV status and thus were used as covariates in the study. MANCOVA's were conducted on the data and produced findings that showed that there were only significant differences in visuo-spatial short-term memory between the two groups. Furthermore, it was also found that there were significant differences between the groups on nonverbal IQ and language proficiency. Therefore, the results showed that HIV may have an overall effect on non-verbal ability and language proficiency and a few aspects of working memory such as visuo-spatial short-term memory. Together with future studies focused on larger sample sizes and children who are not currently on HAART, early developmental interventions can be formulated to assist South African HIV-infected children so that the neurocognitive effects are lessened and their overall lifestyle is improved.

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Chapter 1

Introduction and Literature Review

Introduction

According to Statistics South Africa's (2013) mid-year population estimates, South Africa has a population size of 52.98 million people. Within this population, the Human Immunodeficiency Virus (HIV) prevalence rate is approximately 10%, with 5.26 million people in South Africa being HIV positive (StatsSA, 2013). This makes South Africa the country with the largest number of HIV/AIDS infections in the world. Furthermore, in 2006, one million out of the seven million people with AIDS worldwide were children and adolescents and two million children and adolescents worldwide had died from AIDS worldwide, with 90% coming from developing countries such as South Africa (Pumariega, Shurgart, & Pumariega, 2006). The majority have been infected through vertical transmission of the HI virus from the mother to the infant during pregnancy, birth or breastfeeding or through sexual or drug use risk behaviours in adolescence (APA, 2013). Through Highly Active Antiretroviral Therapy (HAART), infected patients are being treated to decrease onset of AIDS and lower the HIV/AIDS mortality rate and the infection rates (APA, 2013; van Loon, 2009). Highly Active Antiretroviral Therapy (HAART) has dramatically extended the life expectancy of children and adolescents infected with HIV allowing their quality of life, emotional well-being, day-to-day functioning and transition to successful adulthood much more attainable. Despite this, more research needs to be conducted to ensure that this epidemic is controlled and HAART are given and utilised in an effective manner, especially in childhood populations as they comprise the future of any given country (APA, 2013).

Acquired Immune Deficiency Syndrome (AIDS) results in the destruction of the immune system and is caused by the HI Virus. Throughout the three stages of HIV, the virus will attack the T-cells leading to the damage of the immune system. Firstly the patient experiences flu-like symptoms for up to three months with swollen glands as a visible symptom. The virus then progresses to its second phase in which it lies dormant and can persist for an asymptomatic period of up to ten years. The third and final stage is when the patient enters full-blown AIDS and this normally means that the CD4 count is extremely low following which the patient will start to experience secondary illnesses as a result of their weakened immune system (van Loon, 2009). In 2006, the HI virus was the seventh leading cause of

death in children aged 1 to 4 years old and the sixth main cause of death between the ages of 15 and 24 years old in the United States and while this statistic is not known for South Africa, one can infer this is likely to be higher (Pumariega, Shurgart, & Pumariega, 2006). Additionally, HIV progresses more rapidly and is more aggressive in children, thus early identification of their HIV status is imperative (van Loon, 2009).

HIV results in cognitive and motor deficits in children as the severe compromise of the immune system leads to neurodevelopmental dysfunction peri-natally (Ruel, Boivin, Boal, Bangirana, Charlebois, & Havlir, 2011). Neurocognitive deficits affect overall general intellectual abilities and include difficulties with attention and speed of information processing, verbal language, executive –abstraction, complex-perceptual motor function, memory and motor and sensory function (Dawes & Grant, 2007). According to Dawes and Grant (2007) the main memory deficit that is seen in HIV positive patients is with encoding. Long-term storage appears to be less affected, but this is difficult to determine as poor encoding affects storage. While the majority of research has focused on adult populations, a need for research on children is crucial (Angelini et al., 2000; Chang et al., 2001; Farinpour et al., 1999; Martin et al., 1999). This issue will be discussed further later on in the literature review once the HI virus has been explained. Therefore, the aim of this research is to investigate the effects the HI Virus has on working memory in children in South Africa when compared to a matched control group.

Working memory involves the temporary storage and manipulation of information used for a number of tasks in everyday life (Baddeley, 2003). Together, Baddeley and Hitch (1974) proposed a model explaining how working memory processed both visuo-spatial and verbal information through four components, namely, the phonological loop (verbal information), the visuo-spatial sketchpad (visual and spatial information), the central executive which contains the attentional control and finally the episodic buffer which allows for coding of information into long-term memory, as well as providing additional storage space (Baddeley, 2003). This model forms the basis for the current study which compared the working memory profiles of HIV affected and a matched control group of unaffected children.

Working memory and the multicomponent model

Working memory is one of the most stimulating concepts in neuroscience as it is a cognitive faculty essential for mentation and complex behavior. It allows one to interact with the surrounding environment in an effective, flexible and intelligent manner and perform

judgement or executive functioning on changing conditions in one's immediate environment (Dudai, 2002; Gathercole & Alloway, 2006; Payne & Whitney, 2002). Baddeley and Hitch's (1974) working memory model forms the theoretical basis for this study (as seen in figure 1).

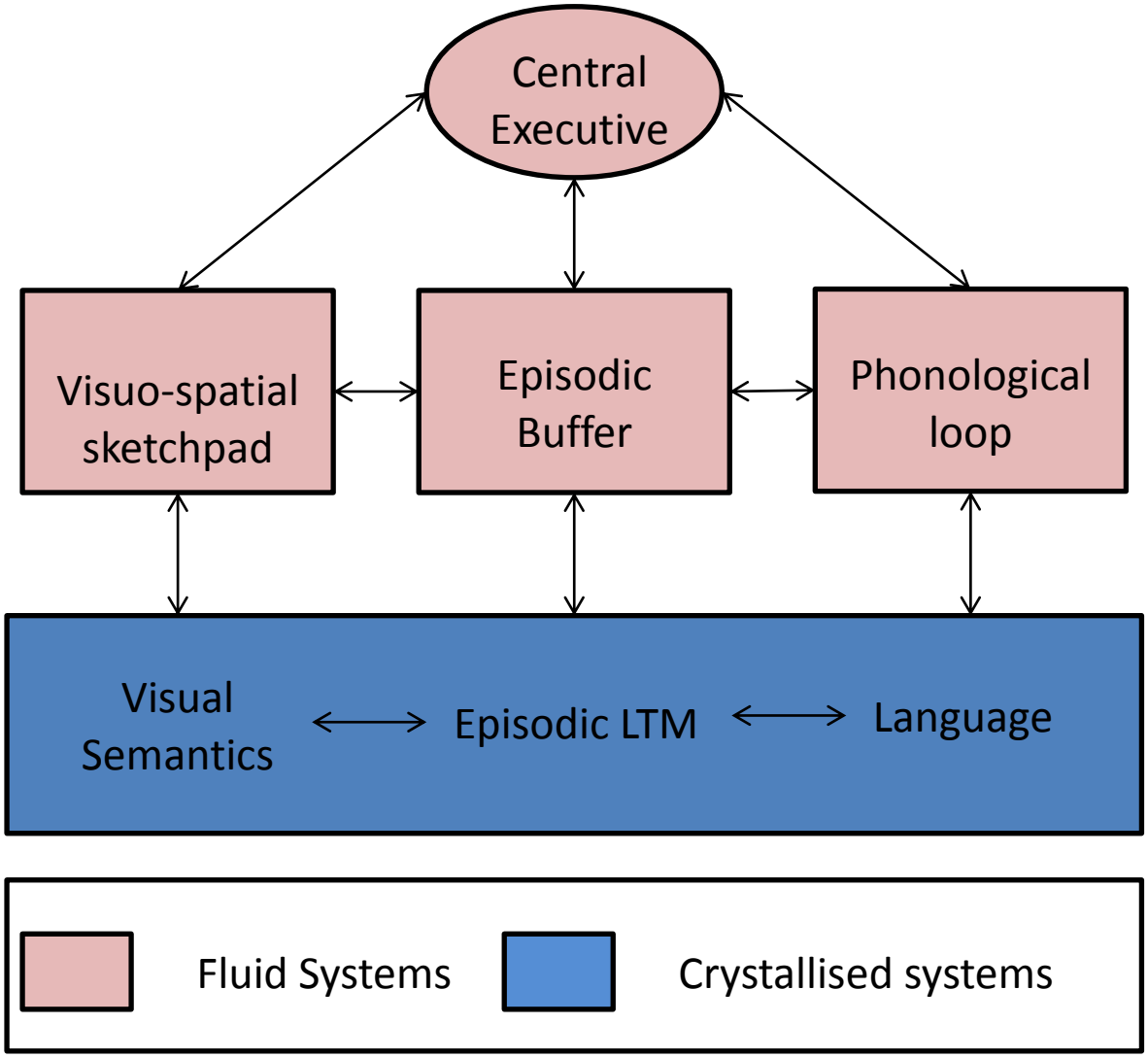


Figure 1. The Multicomponent working memory model. Adapted from "The episodic buffer: A new component of working memory?" by A. D. Baddeley, 2000, *Trends in Cognitive Science*, *4*(11), 418. Copyright (2000) by *Elsevier* Science Ltd. Adapted with permission

This view differs from previous accounts of working memory, such that of Atkinson and Shiffrin (1968), Baddeley and Warrington (1970), Milner (1966) and Shallice and Warrington (1970) in that it is focused on information processing tasks and the functional importance of such a system rather than a system itself as a basic storage capacity (Baddeley, 1996; 2001; 2003; Baddeley & Hitch 1974; Gathercole & Alloway, 2006). These first models were too simplistic and thus required more elaboration, qualification and modification on both the basic mechanisms and representations of memory as newer empirical and theoretical research emerged. This was conducted by Baddeley and Hitch in their multicomponent model for working memory (Miyake & Shah, 1999).

Working memory refers to a system that plays a fundamental role in the temporary maintenance and manipulation of information during performances of cognitive activity, such as comprehension, learning and reasoning (Baddeley, 1986; 1996; 2001; 2007; Dudai, 2002; Gathercole & Alloway, 2006; Siegel & Ryan, 1989). It operates by holding some items in a rapid decay store and retrieving some from the long-term memory store (Siegel & Ryan, 1989). As such, working memory combines attention, short and long-term memory, retrieval, planning and decision-making to create representations of the information at hand (Dudai, 2002; Gathercole & Alloway, 2006). The active representations of information are short-lived, but can be maintained for longer periods of time through active rehearsal strategies. The representations can be subjected to various operations that manipulate the information making it useful for goal-directed behavior (Curtis & Esposito, 2003).

The original concept of working memory developed by Atkinson and Shiffrin (1968) proposed a unitary system which Baddeley and Hitch (1974) elaborated on to form a three component model consisting of two domain-specific subsystems and a limited capacity attentional controller (as seen in figure 1) (Baddeley, 1996; 2001; 2003; 2007; Dudai, 2002). This multicomponent working memory model proposed by Baddeley and Hitch (1974) is empirically based and relies heavily on cognitive memory research with a strong neuropsychological influence (Baddeley, 2007). The two-domain specific subsystems are assumed to store specific information about the items being processed and were later identified to independently deal with acoustic and verbal information, namely the phonological loop, and visual and spatial information, namely the visuo-spatial sketchpad (Baddeley, 1986; Siegel & Ryan, 1989). Furthermore, it was proposed that the working memory system was one of limited capacity that could operate over a range of tasks that involve different processing codes and different input (Baddeley, 1986; 2007; Dudai, 2002).

When compared to other measures of cognitive abilities such as IQ, what is distinguishing about working memory is the limited amount of information that can be stored and processed at the same time rather than the difficulty of the task. Thus, working memory measures are more focused on how much information can be stored and processed at the same time, rather than the difficulty of the task seen in measures of IQ (Gathercole & Alloway, 2006).

A number of working memory models have been proposed in addition to Baddeley's. For example, Cowan's (1999) embedded-processes model, Engle, Kane and Tuholski's (1999) "controlled attention" framework and Lovett, Reder and Lebiere's (1999) ACT-R model all share a similar theoretical framework to Baddeley and Hitch's multicomponent model which focuses on a close link between attention and working memory (Shah & Miyake, 1999). Cowan's (1999) model was formulated to integrate empirical findings on attention and memory and Engle et al.'s (1999) model emphasized the role of the prefrontal cortex in executive control. The ACT-R model focuses on the amount of information that one can simultaneously attend to. Furthermore this was the first model to be based on a computational model followed by the executive-process/interactive control (EPIC) model and the Soar cognitive architecture for working memory created by Young and Lewis (1997). Ericsson and Delaney (1999) developed a long-term working memory framework which examined working memory capacity utilised in everyday skilled tasks. Barnard and Teasdale's (1991) Interactive cognitive subsystems model, on the surface, seems quite different from Baddeley and Hitch's multicomponent model for working memory. However, when the ICS is examined more closely, it is apparent that the three subsystems from Baddeley and Hitch's model, the phonological loop, the visuo-spatial sketchpad and the central executive, can all be mapped onto the ICS framework (Shah & Miyake, 1999).

When the early models were developed, the understanding of the control and regulation of working memory was restricted to pure memorization, such as rehearsal, coding and searching strategies. As research continued, it was evident that the active processing and temporary storage of task-relevant information that dynamically takes place in working memory necessitated a more sophisticated view of these processes. It was formulated that the subsystems are regulated independently but still in relation to each other so that working memory functions as a smooth whole. This is where Baddeley and Hitch's working memory model component of the central executive became important and changed the view of working memory control and regulation to one that was focused more on which mechanisms are controlled and regulated by which components (Shah & Miyake, 1999).

The different models of working memory differ in terms of whether or not working memory is regarded as a unitary or non-unitary system. Some theorists focused on a unitary nature (Engle, Kane & Tuholski, 1999; Lovett, Reder & Lebiere, 1999) yet the majority focused on separate subsystems that comprise working memory (Baddeley & Hitch, 1974; Teasdale & Barnard, 1991). Baddeley and Hitch (1974) theorized a domain-specific set of subsystems and others proposed different types of codes of information. For this research, the domain-specific approach matched theoretical basis of the measurement tool used to assess working memory, further justifying the use of the multicomponent model for working memory.

Lastly, working memory models that will be focused on is the role of working memory in complex cognitive activities. This was the driving force behind the transition from the short-term memory model to the multicomponent working memory model as short-term memory could not account for the ability to process information temporarily whilst performing complex tasks. The most frequently used approach to discuss this is in the context of the chosen model, Baddeley's (1986) model which focuses on the dual-task paradigm. This means that the cognitive task is performed by itself while the secondary task taps into one of the domain-specific subsystems in the model. If the secondary task disrupts the first task, then it usually means that the domain specific subsystem is involved in the performance of the task (Shah & Miyake, 1999).

Baddeley and Hitch's (1974) multicomponent model was chosen out of all the above models as the theoretical model for the current study as the instrument chosen for this research (the Automated Working Memory Assessment) is based on this model's four components, namely verbal (simple) short-term memory, verbal (complex) working memory, visuo-spatial (simple) short-term memory and visuo-spatial (complex) working memory and it is the only standardized tool for non-expert assessors (Alloway, Gathercole, & Pickering, 2006; Alloway, Gathercole, Kirkwood, & Elliot, 2008). Advantages of this instrument include that it is resistant to the quality of social and intellectual stimulation in the home environment, the number of years spent in preschool (which is extremely variable in a developing country such as South Africa), and the financial background of the family (Alloway, 2011; Engel, Santos, & Gathercole, 2008). Furthermore, the multicomponent working memory model has been used in considerable research conducted on both typical and atypical development in children (Henry, 2012).

From experiments, the formation of this multicomponent model for working memory consists of two-subsystems that revealed the capacity to hold a number of digits in a short-term store while simultaneously performing complex cognitive tasks (Baddeley, 1986; 2007). The first system is called the phonological loop and was specifically adapted to retain speech-based material while placing minimal demands on the attentional controller (Baddeley, 1986). The phonological subsystem comprises of a phonological store and an articulatory control process (Baddeley, 1986; 1996; 2003; 2007). This concept of the phonological loop can be used to explain neuropsychological deficits in impaired short-term memory (low digit span) and normal long-term memory functioning (Baddeley, 2002). Most importantly is the interaction between the phonological loop and long-term memory acquisition. This loop provides a platform for the acquisition of language as it allows the information under manipulation to be maintained in order to facilitate the learning of the new material (Baddeley, 2002; 2003). The existence of the phonological loop and its separate storage and rehearsal units is supported by fMRI studies and studies on patients with lesions resulting in phonological loop deficits (Baddeley, 2003). Together the ventro-lateral prefrontal cortex, the dorsolateral prefrontal cortex and the superior parietal cortex aid in the accuracy of verbal working memory tasks (Bunge & Wright, 2007; Dudai, 2002). Furthermore, the storage system is associated with the cortical area, Brodmann's 44, and the rehearsal system is associated with Broca's area (Brodmann's 6 and 40). Consequently activation of the phonological loop is primarily based in the left hemisphere (Baddeley, 2003; Dudai, 2002).

Known as the articulatory loop, this subsystem has two components. The first is articulatory rehearsal, reflected by the word length effect. The word length effect can be explained by subjects being more likely to remember a sequence of words that are short compared to words that are long but of equal frequency in the language and is analogous to subvocal speech (Baddeley, 1986; 2003; Baddeley, Chincotta, Stafford, & Turk, 2002). This is based on the simple concept that longer words take longer to articulate and thus reduce the rate at which the item can be rehearsed. Furthermore the word length effect suggests that the capacity of the phonological loop is determined by the temporal duration of spoken words and the memory span is determined by the rate of rehearsal (Baddeley et al., 2002). The second aspect of this articulatory system, the phonological store, is associated with speech perception and can be explained through the word similarity effect (Baddeley et al., 2002). This effect shows evidence for the role of the phonological loop in short-term memory tasks and that recall is 25% worse when the words are phonologically similar to one another

(Larsen, Baddeley, & Andrade, 2000). Through auditory presentation or visual representation, words are stored into a short-term store and are maintained and refreshed by the process of articulation (Baddeley, 2003). Strengths of the phonological loop is that it can provide a temporary sequential storage, using a process that is rapid and requires minimal attention but a disadvantage to this subsystem is it is a very limited component of working memory (Baddeley, 2012).

The second working memory subsystem, the visuo-spatial sketchpad, works to simultaneously maintain both visual and spatial information and is limited in capacity to hold roughly three to four objects (Baddeley, 2003). This system retains and manipulates images and is susceptible to disruption when concurrently processing spatial information regarding visual images (Baddeley, 1986; 1996). Evidence from neuropsychological and functional imaging has proven a similar multicomponent system for the visuo-spatial sketchpad as for the phonological loop however it forms an interface between two separate types of information, visual and spatial. The visuo-spatial sketchpad allows one to solve for visuo-spatial problems primarily through the use of the long-term memory store (storage is controlled visually or spatially) and sometimes through the use of the senses (storage is controlled through motor and kinesthetic elements) (Baddeley, 2002; 2003). Neuro-anatomically, the visuo-spatial sketchpad is principally controlled by the right hemisphere of the brain (Baddeley, 2003). Occipital lobe activation is noted when visual stimuli is encountered while parietal regions are accessed when spatial interactions occurred. Most importantly for the co-ordination and control of both sets of stimuli, the frontal lobes are triggered (Baddeley, 1996; 2002). More specifically, the dorsolateral prefrontal cortex seems to be more involved in spatial working memory in humans and fMRI studies have identified the superior frontal sulcus (SFS) and the intra-parietal sulcus (IPS) as being highly active in children during visuo-spatial working memory tasks and the increased interaction between them is extremely important in the improvements of a child's visuo-spatial sketchpad towards effective adult functioning (Bunge & Wright, 2007; Luciana, Conklin, Hooper, & Yarger, 2005). One such issue with this subsystem is the dissociation between visual and spatial working memory through multiple demonstrations by research investigations and neuroimaging studies (Klauer & Zhao, 2004; Smith & Jonides, 1997). Further issues have been raised about the nature of rehearsal in the sketchpad and thus it is proposed that further investigation into this subsystem must be conducted (Baddeley, 2012).

The third component of Baddeley and Hitch's (1974) multicomponent model is the limited capacity attentional controller referred to as the central executive. In the early definitions of this sub-system, it was suggested to be a homunculus, a "little man" who made the decisions about how the subsystems should be used (Baddeley, 2003). More recently, the roles of the central executive have been defined as the capacity to exert control functions, focus attention and divide attention. The latter role of the central executive, determined by examining evidence from patients with frontal lobe damage, revealed the ability to switch attention from one stimulus to another through the use of the central executive (Baddeley, 2002; 2007; Siegel & Ryan, 1989). Therefore the central executive is the most important aspect of working memory, yet it is the least understood one (Baddeley, 2003).

The fourth and final component of the multicomponent model of working memory came from a fourth role proposed for the central executive which allowed the long-term store to interact with the individual sub-systems while continuing to actively maintain and manipulate information across all stores. The episodic buffer addressed these problems of the working memory model by representing a multimodal coded storage system (Baddeley, 2002; 2003). The term 'episodic buffer' came from two distinct properties: the structure is episodic in that it holds integrated scenes of episodes of information and it is a buffer in the sense that it provides a limited capacity 'backup' system using different codes (Baddeley, 2002; 2007). However the episodic buffer itself has no storage capacity (Baddeley, 2007). Lastly, the flow of information in Baddeley's working memory model is bi-directional in that the subsystems assist and are connected to long-term memory but they are also affected by long-term implicit knowledge of language and the visuo-spatial world with which people interact every day (Baddeley, 2002).

Neuro-anatomy of working memory

Given the complex nature of working memory and its primacy in this study, it is essential that its neuroanatomical bases are investigated further (Goldman-Rakic & Leung, 2002; Yeo, Hill, Campbell, Vigil & Brooks, 2000). Cognitive psychologists have been able to localise theoretical concepts such as working memory in the brain, mainly the frontal cortex, by working together with neuropsychologists conducting neuroimaging studies and examining brain damaged patients (Braver, Nystrom, Jonides, Smith, & Noll, 1996; Curtis & Esposito, 2003; Goldman-Rakic & Leung, 2002; Yeo et al., 2000). This is especially noted in Baddeley and Hitch's (1974) working memory model which proposes a multicomponent

system involving a selection and executive control center, the central executive and maintenance modality-specific slave buffers. Through studies using both Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI), Braver et al. (1996) and Goldman-Rakic and Leung (2002) acknowledge the psychological distinction between the storage and processing components within working memory and propose that the prefrontal cortex is topographically organized into information constrained domains, allowing each domain-specific network to have a central processor with integrated storage and processing units. These studies also link multiple brain regions that sub serve the prefrontal cortex in working memory such as the posterior parietal cortex, the basal ganglia, the anterior cingulate, left anterior area and Broca's area through examining working memory tasks and working memory impairments in brain damage patients (Braver et al., 1996).

More specifically, both the dorsolateral and ventro-lateral prefrontal cortex are seen as critical elements for various types of working memory tasks (Curtis & Esposito, 2003; Dudai, 2002; Goldman-Rakic & Leung, 2002; Luciana, Conklin, Hooper, & Yarger, 2005). Both are involved specifically in the executive control of working memory (central executive) (Ward, 2010; Zillmer, Spiers, & Culbertson, 2008). In addition to these dorso-ventral dissociations, lateralization has been proposed as a contributing factor to working memory function. Findings from Braver et al. (1996) revealed bilateral activity in the middorsolateral area with the left inferior region (LIFG) consistent with Broca's area being activated in tasks requiring verbal rehearsal. Neuroimaging work has revealed a dissociation between areas of the lateral prefrontal cortex that mediate information maintenance, which are more ventrally located and those that facilitate self-monitoring which allows the information to be manipulated and controlled by the executive components, which are dorsally located (Luciana, Conklin, Hooper, & Yarger, 2005). Thus, representations in working memory are associated with the activation of the prefrontal area 46 of the dorsolateral prefrontal cortex, whereas maintenance in working memory activates the prefrontal area 8 and the intra-parietal cortex (Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000).

The prefrontal cortex is not the sole contributor to working memory function as neural systems extend and interact with distant cortical areas including the posterior parietal cortex, the infero-temporal cortex, the cingulate gyrus and the hippocampus, although the exact nature of these interactive networks are still being researched (Curtis & Esposito, 2003; Goldman-Rakic & Leung, 2002). According to Dudai (2002), the functional determinants of the specialization may relate to the type of information processed, the role in maintaining the

representation throughout the task as opposed to the selection of information from other brain areas and to the characteristics of multiple types of information. This means that the involvement of the distant cortical regions mentioned above depends on the function (selection or maintenance) needed in working memory and the type of information being processed.

Working memory, a complex cognitive system, requires simultaneous processing of incoming new material and the retrieval or old implicit information (Siegel & Ryan, 1989). The limited capacity element of this model implies that the greater the task demands on the central executive, the less processing space and cognitive energy will be available for the two domain specific subsystems (Baddeley, 2007; Siegel & Ryan, 1989). This aspect of working memory is extremely important for individuals with learning difficulties or disorders that place extra strain on their cognitive ability and marks the reason for working memory dysfunction in these individuals. Since HIV positive children are known to have learning problems, this is relevant to the sample of this study. Later on the effect of the HI virus and the learning implications as a result of this virus will be discussed in relation to working memory.

Neurodevelopment of working memory in learning

A significant way in which behavior changes over childhood is the focus on goals and the improved ability to ignore distractions (Bunge & Wright, 2007). The development of the prefrontal cortex throughout these years is relevant to the current study. The prefrontal cortex coordinates high-level cognitive functions that assist this goal directed behavior. In order to reach these goal-directed behaviours, functions such as inhibitory control, the ability to integrate past knowledge with future goals and behavioural flexibility are all developed and mastered. By definition, future-directed behavior is integrative, meaning it requires one to ignore distractions and focus on pertinent information that will translate into goal-directed representations. In essence what this requires is an effective working memory. The central executive allocates attentional resources to manipulate the information that is maintained by the subordinate systems, the phonological loop and the visuo-spatial sketchpad and strategies are implemented for the relevant use of the information (Luciana, Conklin, Hooper, & Yarger, 2005). Working memory develops progressively from birth to 16 years. Studies on the development of working memory in young children have been informative on this progression (Gathercole, Pickering, Ambridge, & Wearing, 2004; Luciana, Conklin, Hooper,

& Yarger, 2005). Working memory performance gradually improves during preschool into middle children where children are required to keep multiple responses in mind and shift responses among them. In middle childhood, executive control over information appears to increase in precision consistently, further justifying the age choice for this study (Luciana, Conklin, Hooper, & Yarger, 2005).

According to Gathercole, Pickering, Ambridge, and Wearing (2004) and Siegel and Ryan (1989), a maturational linear increase in size of each working memory component's capacity has been demonstrated between 4 years old to early adolescence. Functional MRI studies show that working memory circuits and the components of Baddeley's working memory model are not only in place by age 6 but are also strengthened individually. The phonological loop and visuo-spatial sketchpad are closely linked to the central executive, yet independent of each other and this structural organisation constantly continues throughout childhood (Bunge & Wright, 2007; Gathercole et al., 2004). There is evidence to suggest that visuo-spatial skills are more intact in early childhood as the child develops spatial recognition of their environment and other important aspects of development such as facial orientation and recognition, yet as the child begins formal school, the verbal working memory functioning develops more as the need for skills such as language and comprehension are more imperative in middle childhood (Gathercole & Pickering, 2000). Both the visuo-spatial aspect and the verbal aspect of working memory are controlled through the central executive to ensure a fully functioning working memory system as proposed by Baddeley and Hitch (1974). Furthermore, increased activation in the frontal, parietal and striatal regions of the brain results in improvements in the central executive over the course of middle childhood.

The present study's focus is on working memory functioning in HIV positive children. These children are at risk for neuro-dysfunction (Semrud-Clikeman &Ellison, 2007). More importantly these difficulties become apparent during the acquisition of new learning material and thus it is vital to identify and provide appropriate interventions that will assist the child as he/she begins formal schooling (Gathercole & Alloway, 2006). Attentional focus and executive functioning deficits are common in children with HIV (Lowenthal, Cruz, & Yin, 2010; Semrud-Clikeman & Ellison, 2007; Tomasi, Chang, Caparelli, & Ernst, 2007). This is extremely important between the ages of 5 to 12 years where developmental milestones such as composing sentences, recalling parts of a story, learning to read and planning or solving a problem are expected (Lowenthal, Cruz, & Yin, 2010). Furthermore, increased activation in the frontal, parietal, and striatal regions of the brain results in

improvements in, not only cognitive control, but specifically working memory over the course of middle childhood in typically developing children. This increased activation across developmental changes in the brain has been generalized as a movement from diffuse to focal activation allowing for the working memory components to strengthen. However, the exact pattern of change is specific to the tasks being examined, the ages under observation, and most importantly the brain area or construct in question (Bunge & Wright, 2007).

A study conducted by Swanson (1993) found that working memory problems were common among students with learning disabilities and have been found to be related to the neurological degradation caused by HIV. Additionally the learning deficits examined in previous studies on working memory and HIV failed to identify specific verbal or visuo-spatial working memory difficulties, but rather a global decrease in performance as a result of central executive problems. This is seen in a study conducted by Bagenda et al. (2006) assessing the health status and neurodevelopmental progress of HIV-positive school-age (6 to 12 years) children who were not receiving ARV's. Twenty-eight infected, ARV-naïve children, 42 sero-reverters and 37 HIV-negative children were selected and matched on age and gender. They underwent evaluations of their health, neurological wellbeing and psychometric wellbeing. The Kaufman-Assessment Battery for Children (K-ABC), measuring intelligence and achievement, and the Wide Range Achievement Test 3 (WRAT-3), measuring basic skills needed for reading, spelling, and arithmetic, were used to assess the children. This study found global cognitive effects rather than specific effects in the children infected with HIV.

The HI virus, initially thought to only affect the immune system, has subsequently been found to have a direct impact on the central nervous system causing the development of a number of CNS-related diseases and disorders. The impact on the CNS manifests in a number of ways ranging from mild cognitive impairment of general fluid intelligence to severe deficits in specific cognitive domains such as in attention, memory, executive function, and motor and sensory function (Dawes & Grant, 2007; Webster, 2009). Proposed mechanisms for the pathogenesis of the HIV in the CNS of children includes direct neural injury, macrophage destruction resulting in neurotoxicity, dysfunction caused by viral products, neuroreceptor blockade, co-infection with other agents, autoimmune reactions, antibody-mediated cellular toxicity, integration of the provirus in the CNS cell lines, alteration of the blood-brain barrier, and brain vascular changes (Pumariega, Shurgart, & Pumariega, 2006). A number of vascular lesions ranging from aneurysms to infarctions have been found using

neuroimaging studies as well. Furthermore, HIV results in three patterns of neurocognitive developmental abnormalities, namely: 1) rapid progressive encephalopathy, 2) sub-acute progression of encephalopathy with relative stable periods and 3) static encephalopathy with a failure to achieve new milestones. Further Computerized Tomography (CT) scans identify cortical atrophy, ventricular enlargement and white matter changes in HIV affected individuals (Brown, Lourie & Pao, 2000). Autopsy studies reveal decreased brain weight, inflammatory changes, calcifications of the basal ganglia vessels, white matter deterioration and astrocytosis (Pumariega, Shurgart, & Pumariega, 2006). All of which affect the anatomical areas of the brain responsible for memory and specifically working memory including the lateral frontal lobes, the amygdala, the hippocampus and the thalamus. Furthermore, the primary visual cortex, the temporal regions and the parietal regions are all implicated in visuo-spatial memory due to their association with spatial mapping, object categorization and orientation and Broca's area is associated with verbal working memory as it controls the processing of verbal information (Ward, 2010; Zillmer, Spiers, & Culbertson, 2008).

Human Immunodeficiency Virus (HIV)

The human immunodeficiency virus is an infectious disease that attacks the central nervous system through the blood-brain barrier (BBB) (Smith, Adnams & Eley, 2008; Wiley, et al., 1991). The neurological problems include a collection of impairments arise ranging from psychomotor slowing with personality changes and impaired memory to severe cognitive and motor disturbances (Wiley et al., 19991). The HI virus is not like any other virus as the human body's immune system is unable to get rid of it and it continues to break down your CD4 cells until the body can no longer fight the secondary infections and diseases anymore. HIV-1 is a retrovirus that produces profound CD4 depletion. This could be attributed to the initial depletion of gut-associated memory T cells. It is followed by a chronic immune activation which results in the fatigue of homoeostatic T-cell responses and progressive immunodeficiency. The CD4 receptor is the main target for HIV-1 infection. The HIV-1 strains are named according to the preferred site of replication for instance the T-tropic viruses replicate in the T lymphocytes whereas the M-tropic viruses replicate in macrophages (McArthur, Brew, & Nath, 2005). These are the pathways for the virus to reach the blood brain barrier explained below.

There are three distinct pathways that allow for the virus to reach the blood brain barrier, these include: macrophages-monocytes and/or CD4+ T lymphocytes, through the cerebral micro vascular endothelial cells (CMVECs) by transcytosis and direct infection of newly formed HIV viral particles into the cerebral compartment. Following the integration of the HI virus into the host-cell genome, it can remain latent for years. At this point in time, the cellular function does not appear to be affected. Through cellular activation, the virus produces retrovirus mRNA. The reason for the devastating effects the HI virus has on the brain can be attributed to the protection of the blood brain barrier. It prevents penetration of antiretrovirals and thus provides a sanctuary for the HIV to replicate uninterrupted. This virus enters the nervous system soon after infection and thus the detrimental effects are seen in the neurological dysfunction in both children and adults infected with HIV (McArthur, Brew, & Nath, 2005).

HIV affects the nervous system both directly and indirectly. Direct effects lead to neurological and neurocognitive manifestations which are advanced by resource limited environments and indirect effects are seen as a result of immunodeficiency leaving the body susceptible to secondary opportunistic infections which are detrimental to children in South Africa (McArthur, Brew, & Nath, 2005; Smith, Adnams & Eley, 2008). The most common neuropathological changes are seen in the basal ganglia, brain stem and deep white matter and it has been shown that a decrease in brain density is seen in 40% of the frontal and temporal lobes and about 50-90% within the hippocampus in adults (McArthur, Brew, & Nath, 2005). Furthermore, the most detrimental consequence the HI virus has on children is the CNS complications, including cerebral atrophy, especially myelinopathy of the prefrontal cortex, pyramidal tract signs and calcification of the basal ganglia (Fishkin et al., 2000; Pumariega, Shugart, & Pumagiera, 2006). This implies similar complications seen in both children and adults, but because the development of the CNS is crucial in childhood, the developmental effects HIV has on children is more detrimental than adults.

Despite the high prevalence rates of HIV infection, relatively few studies have looked at the cognitive functioning of HIV positive patients, especially children, in African countries (Robertson, Nakasujja, Wong et al., 2007). Further, the generalizability of cognitive difficulties of HIV positive patients from Africa with developed country patients cannot occur due to the vast differences in resource settings and influencing factors such as socioeconomic status (SES) as the majority of children infected with HIV come from impoverished backgrounds with poor nutrition, health care and the varying strains of the HI

virus (Fischkin et al., 2000; Robertson, Nakasujja, Wong et al., 2007). Another important factor to consider is that South Africa contains a separate clade of HIV as opposed to the developed world. Clade C, the more aggressive clade, is the predominant clade of the HI virus found in Southern Africa, whereas the infections in the Americas, Europe, Japan and Australia tend to be clade B (Le Vu et al., 2010). This further affects the progression of the virus, the resistance to medication and thus the overall knowledge surrounding this type of HIV (Cairns, 2008).

In 1983, the first child infected with the HI virus was described followed by a global epidemic affecting the health and survival of children worldwide. A child is most commonly infected with this infectious disease through vertical transmission from the mother. This usually occurs in utero, intrapartum (through exposure to the mothers blood products or transfusions), or post-partum through breastfeeding. Furthermore, the post-partum vertical transmission contributes to between 30% and 50% of all vertical transmission in children and can be prevented through timely maternal treatment with HAART (Pumariega, Shurgart, & Pumariega, 2006). Seventy-nine percent of children infected perinatally through vertical transmission remain relatively asymptomatic for several years and usually experience the onset of AIDS at a mean age of 6.1years (Fishkin et al., 2000). This further emphasizes the need for research in this area and age group, especially in third-world regions where these advances are lacking.

HIV has a detrimental effect on the cognitive functioning of a child as the virus attacks the CNS. Additionally, certain factors such as malnutrition, poor pre-natal and post-natal care, pre-natal insults and other diseases such as strokes or neoplasms, affect the neuropsychological functioning of the CNS in these children (Pumariega, Shurgart, & Pumariega, 2006). Furthermore children with HIV may be distractible, impulsive and unorganized (Lowenthal, Cruz, & Yin, 2010).This neurocognitive deterioration is associated with the increased replication of the HI virus, usually resulting in HIV-progressive encephalopathy (HIV-PE). Human Immunodeficiency Virus-Progressive Encephalopathy is associated with a triad of symptoms including impaired brain growth, progressive motor dysfunction and a loss or plateauing of developmental milestones (Pumariega, Shurgart, & Pumariega, 2006).

When assessing the neuropsychological impact of HIV, large differences in developmental deficits, progression and severity of disease are seen in an adult as opposed to a child brain.

This is due to the perinatal transmission of the virus occurring when the immune system is at its most vulnerable as it is still undergoing development. Typically, children infected perinatally show more severe manifestations of CNS disease early on life and a more rapid progression of the disease than adults (Webster, 2009). It follows that HIV will have an effect on school functioning. Lack of attendance due to secondary illness as a result of the disease results in chances of the child falling behind his/her classmates and thus affects their academic development. Secondly, the virus affects the energy levels of the child and thus restricts them from participating in school activities fully. Therefore, the culminating effect of all these aspects as a result of HIV can be potentially damaging to the cognitive functioning and academic advancements of the child (Brown, Lourie, & Pao, 2000; van Loon, 2009).

Through HAART, infected patients are being treated to decrease the onset of AIDs and lower the HIV/AIDs mortality rate and most of the individuals with HIV rely on the government health services for their medication (Bachmann & Booysen, 2004; van Loon, 2009). It is for this reason that the sample for this study was sourced from a government-funded hospital currently providing free HAART. When looking at the overall effects of HIV on a patients wellbeing and life predictions, the cognitive deficits that a child has will negatively impact their future employment and their abilities to run a household later on in life due to HIV being a chronic disease rather than a fatal one (Robertson, Nakasujja, Wong et al., 2007; Scandlyn, 2000). Identifying these deficits in childhood will aid in the preparation and implementation of training to help alleviate symptoms alongside the HAART. Part of this identification involves identifying developmental delays, for e.g. children aged 4 years and older, show delays such as the inability to concentrate on a single activity for more than 5 minutes, the inability to understand a two-part command and any developmental age-appropriate milestone. Health care professionals and parental care givers must acknowledge and monitor such delays to ensure appropriate treatment and rehabilitation can be given (Lowenthal, Cruz, & Yin, 2010).

Working memory deficits in HIV positive children

Working memory deficits have been identified in HIV positive children, especially visuo-spatial problems, interference with executive control functions such as planning, and implementing complex behaviours. Domain specific deficits in visuo-spatial processing, visuo-motor integration and fine-motor skills have all been noted in children with HIV (Lowenthal, Cruz, & Yin, 2010; Semrud-Clikeman & Ellison, 2007; Tomasi et al., 2007).

These deficits manifest themselves through difficulties with mathematics, poor handwriting, and problems completing certain activities of daily living such as getting dressed. Furthermore, these domain specific deficits relate to abnormalities within the brain's white matter, frontal system, and basal ganglia and further justify the use of Baddeley and Hitch's (1974) multicomponent model for working memory as it includes all domain specific tasks (Lowenthal, Cruz, & Yin, 2010). Although Alloway et al., (2009) discovered that is better to investigate working memory deficits through domain-general components, like the central executive, rather than the domain-specific visuo-spatial sketchpad and the phonological loop, for the purpose of this study, all four aspects of the multicomponent model were assessed in order for a full working memory profile to be defined for HIV positive children and compared to that of a control group.

With regards to the HI virus and working memory, the virus results in a number of cognitive abnormalities, more importantly neuropsychological deficits to the central nervous system that can be seen in patients with HIV include a decrease in sustained attention, a lack of mental flexibility and poor memory with evidence of the frontal brain regions being activated in fMRI studies (Martin et al., 1999; Chang et al., 2001; Tomasi et al., 2007). Moreover, a diffuse deficit in HIV is seen across all types of information and types of working memory processes (Angelini et al., 2000; Martin et al., 1999). Differing from adults, children with HIV show almost exclusive CNS damage, sparing the peripheral nervous system and affecting the whole brain rather than the spinal cord. Reports show progressive encephalopathy and spastic paraparesis as the main neurologic disorders found in HIV-positive children (Angelini et al., 2000).

Fishkin et al. (2000) investigated the neurodevelopmental effects of perinatally acquired HIV infection on children in preschool in the United States. Forty children aged 3 to 5 were matched to non-infected controls on age, sex, and prenatal drug exposure. These children were tested on the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R). The results showed a lack of gross cognitive deficits when infected participants were compared to controls, yet more focal deficits were seen. They proposed that an investigation in older children should be conducted and this further warrants the need for a study such as the current one (Fishkin et al., 2000). This study's results are contradictory to what has been proposed in other previous research (Koekkoek et al., 2008; Ruel et al., 2011; van Loon, 2009). Reasons for this may be related to the drug exposure aspect of this study as well as the fact that certain children were bilingual in the study and the authors refer to a number of

factors that affect outcomes in studying cognitive functioning in children which include the fact that the children with HIV come from the minority and low socio-economic status populations in the USA (Alloway et al., 2009; Fishkin et al., 2000).

Farinpour and colleagues (1999) included 30 HIV positive (15 seropositive asymptomatic (mean age = 41.8years) and 15 seropositive symptomatic (mean age = 41.5years)) and 30 HIV negative (mean age = 39.4years) males in their study. The participants all shared a drug abuse history and were enrolled in a larger study investigating the overall effect of HI infection in cognitive function completed the listening span test and the self-ordered pointing test. The study found evidence for verbal, spatial and auditory working memory deficits in HIV positive patients compared to the equivalent control groups. They continue to express the need for more research examining the relationship between working memory and HIV as it is critical to the management of the disease and is essential to determining clinical use of working memory measures. Both studies were completed only on adult male populations, thus the results cannot be compared to these children populations, yet the effect of the HI virus on an adult is important to consider when looking at childhood populations.

A Ugandan study on 93 HIV positive and 106 HIV negative African children aged 6-12 years, conducted by Ruel et al. (2011), found that there were significant deficits in total motor proficiency and cognitive deficits in visual reaction times, sequential processing, simultaneous processing, planning/reasoning, global performance in HIV positive children when compared to healthy controls. The HIV positive children were compared to the HIV negative children on the Test of Variables of Attention (TOVA), K-ABC and the Bruinink-Oseretsky Test for Motor Proficiency. Another study conducted in South Africa examined the cognitive functioning of children infected with HIV compared to healthy controls (van Loon, 2009). Eighty one HIV positive children were compared to 86 HIV negative children on all three sets of the Raven's Coloured Progressive Matrices (A, Ab and B), and the results showed significant lower performance in the Raven's in the HIV positive children compared to the controls. Critiques of this study include small sample size and the use of a population that was not first language English speakers and thus translators were sometimes used (van Loon, 2009). Both of these studies concur with previous research showing cognitive deficits in HIV and children and similar results were thus expected in the current study (Alloway et al., 2009).

Finally Koekkoek et al. (2008) conducted a study on 22 peri-natally HIV-infected children (mean age = 9.46 years). They administered intelligence tests followed by a series of neuropsychological tests from the Amsterdam Tasks program such as the Attentional Network Test (ANT). The children all performed within the average range with regards to the general intellectual functioning but neurocognitive deficits were seen in executive functioning, working memory and processing speed. The most severe deficit was seen in executive function (attentional flexibility and visuo-spatial working memory). Once again this study shows results that are in line with previous research. It is limited by a small sample size, however (Alloway et al., 2009; Koekkoek et al., 2008). Thus to the researcher's knowledge, there are no studies comparing verbal and visuo-spatial working memory functioning in young children with HIV/AIDS to healthy controls in South Africa. This makes the current study innovative and it addresses an important area of functioning in school-age children.

Covariates in the investigation into working memory and HIV in children

Findings from second language studies indicate that verbal working memory is an effective predictor of second language vocabulary development, second language proficiency and, more importantly, it plays a more crucial role in second language (L2) than first language (L1) acquisition (Payne & Whitney, 2002). Since the majority of participants in the current study were English L2 learners, verbal working memory is likely to be affected. Therefore it was necessary to include a separate measure of language proficiency in this study. Furthermore, the deterioration of language skills, expressive more than receptive language, is commonly seen in children infected with HIV. Consequently, the periodic evaluation of children's language development should be a regular aspect of the overall HIV status monitoring. It will assist the clinicians in evaluating the progression of the illness and the effectiveness of the prescribed treatment (Pumariega, Shurgart, & Pumariega, 2006).

An evaluation of language can be conducted through a concept linked to working memory known as elicited imitation (EI). Elicited Imitation is a known testing method for language competence where the participant is verbally presented with a series of sentences and then they are expected to imitate the sentences as accurately as possible. The Sentence Repetition Test (SRT), used as the measure for language proficiency in the current study, uses EI as the form of assessment. Short-term memory, long term memory and working memory are all associated with language competence, but in this study where the tasks were given in English

to second-language learners, heavy demands are places on both working memory and long-term memory. Working memory plays is implicated as the participants have to actively maintain and perform the task given to them, implying that working memory and language competence are not independent (Okura & Lonsdale, 2012).

This language competence task utilises the phonological loop from Baddeley and Hitch's (1974) working memory model, and so, a correlation between these variables was expected (Baddeley, 2003). More specifically, the articulatory loop plays a fundamental role in the testing method of EI. EI has two main characteristics: firstly it is time-constrained and thus prevents the articulatory loop being used and thus working memory cannot be enhanced. Furthermore the repetition aspect of EI allows for deliberation of the grammatical issues to be less noticeable. This creates a test that measures implicit rather than explicit language. Lastly, EI measures verbal STM performance in the form of knowledge of various linguistic elements rather than rote memory ability and working memory is essential to performing well on an EI test; indicating the importance of the inclusion of this variable as a confounding variable to this research study (Okura & Lonsdale, 2012). Additionally executive function, or what Baddeley refers to as the central executive, pays a critical role in second language production and comprehension, implying the imperative link between working memory, HIV and language proficiency in this study (Payne & Whitney, 2002). This link between language competence, HIV and working memory is important to note as all interact with each other and play a role in the results of this study. The second covariate that the current study included was a measure of non-verbal intelligence. With reference to previous research, the effects HIV has on a child's cognitive ability tend to be more generalized rather than specific deficits. Thus in order to compare the groups effectively, they need to be comparable in terms of IQ, particularly since there a link between non-verbal ability and working memory (Baddeley, 2003). This is why non-verbal intelligence was measured by the Raven's Coloured Progressive Matrices (RCPM).

It is evident that working memory provides a crucial interface between perception, attention, memory and action (Baddeley, 1996; Baddeley 2003). Together with the development of a wide range of validated measures of working memory such as the Automated Working Memory Assessment (AWMA) and the understanding of working memory profiles in an atypical population such as children with HIV, it would allow for the development of effective interventions (Alloway, 2007; Alloway, Gathercole, Kirkwood, & Elliot, 2009). Therefore the purpose of the study was to investigate the working memory profiles of both an

HIV positive children and a control sample, on cognitive tasks (Automated Working Memory Assessment), general intellect tasks (Raven's Colored Progressive Matrices) and language competence tasks (Sentence Repetition Test).

Chapter 2

Methods

Research design

The study compared the working memory profiles of HIV positive children with that of a matched control group. There were four variables under investigation: one independent variable (HIV status), four dependent variables (working memory functioning i.e. verbal short-term memory, visuo-spatial short-term memory, verbal working memory and visuo-spatial working memory) and two covariates (non-verbal intellectual ability and language proficiency). The instruments used in this study were all standardized measures used to quantify working memory function, non-verbal intellectual ability and language proficiency. Furthermore, since the instruments yielded numerical data, this study was quantitative in nature. None of the variables in this study could be manipulated and thus a non-experimental design was applied to this research. In addition, this study was conducted at one point in time and with an intention to compare the effects of the presence or absence of the independent variable (HIV) on the dependent variable (working memory). Thus, the design of this study was a cross-sectional, between groups, ex-post facto and non-experimental.

Participants and sampling

Fifty two participants (26 in the HIV positive group and 26 in the control group) were tested. They were aged between 6 and 8 years old, which is when the child's social and learning outcomes are vulnerable to external and internal influences. The descriptive statistics for the sample can be seen in Table 1 below where no significant difference was seen between the two groups in terms of age.

Table 1

Descriptive characteristics of matched groups of children with HIV/AIDS and control group

		HIV positive (n = 26)			Control (n = 26)		
		N	Mean	SD	N	Mean	SD
Age		26	6.58	.76	26	6.73	.92
Gender	Males	11			11		
	Females	15			15		
SRT		26	7.23	6.89	26	18.08	7.77
RCPM		26	11.96	4.16	26	19.62	5.63

Notes. SRT = Sentence Repetition Test, RCPM = Raven's Colour Progressive Matrices

Between the ages of 6 and 9 a child is exposed to learning numeracy and literacy in formal schooling that, through the use of working memory, develops rapidly. Thus working memory is one of the most malleable and evolving constructs. When a child begins formal schooling, neurodevelopmental deficits are often discovered. Therefore early identification is essential to assist these children and their overall cognitive, psychosocial and educational functioning. Furthermore, being a developing country, South Africa exposes children younger than 5 years to multiple risks. Some of these include poverty, SES status, malnutrition and un-stimulating home environments (Fishkin et al., 2000; Grantham-McGregor, Cheung, Cueto, Glewwe, Richter, & Strupp, 2007). Thus, the impact of these factors on the main construct in this study, working memory functioning, is important to control as far as possible.

In order to do this, the researcher employed a control group from the same socioeconomic bracket as the HIV positive group. But it must be noted schooling grades could not be used as appropriate control measures as children from South Africa are not necessarily placed in the correct grade for their age. The age group chosen for this research (middle childhood) is essential to further developing the knowledge surrounding working memory as this is when the working memory abilities are starting to be consolidated (Bunge & Wright, 2007). Furthermore according to Fishkin and colleagues children infected with HIV older than 5 years have a strong likelihood of developing greater cognitive deficits as the disease progresses. This presents another urgent reason for studies such as this one that can allow for early detection of dysfunction (Fishkin et al., 2000). Due to the vast differences between the populations that enter the hospitals, one-to-one matching across the two groups could not be practically obtained. Therefore the matching between groups 1 and 2 was on a collective level.

Inclusion criteria

The participants and their legal guardians were asked to participate in the study providing they satisfied the following criteria:

- Age: born between 2004 and 2007. It is difficult to rely on the grades of the children as many children may enter a grade earlier than expected or may be repeating a grade. The participants in the study were in grades R – 3.
- Attendance at a mainstream school (i.e. not a special needs school).

- Group 1- HIV positive group: the participants in this group had to be on antiretroviral medication and thus their medical records showed they were HIV positive, had been virally suppressed for 6 months and whether they were on their first or second line treatment. This information was found by analyzing their viral load and CD4 counts from their previous doctor's visit report with appropriate consent from a legal guardian.
- Group 2-HIV control group: the second group in this study included children who were HIV negative and came from an HIV negative mother. This was assumed by identifying the mothers HIV status through her medical records with her consent.

Exclusion criteria

Participants were excluded according to the following criteria:

- Group 1 and 2: children with any form of neurological compromise such as Epilepsy, Meningitis and Traumatic Brain injury were excluded from the study to prevent any confounding effects of the neurological impairments of the HI virus on the test.
- Children attending special needs schools were also excluded as this indicates an already compromised cognitive ability.
- Lastly, the presence of an incapacitating illness, such as Bronchitis, TB, pneumonia, etc., that leads to the child under performing on the tests were also excluded from the study as their cognitive abilities at that point in time were reduced greatly by secondary illnesses owing to their HIV positive status.

Instruments

Four instruments were used, namely, a demographic questionnaire, the Automated Working Memory Assessment (AWMA), the Raven's Coloured Progressive Matrices (RCPM) and the Sentence Repetition Test (SRT). None of the tests have been standardized on a South African population, which is also why a control group was included.

Demographic Questionnaire. (Refer to Appendix A). The demographic questionnaire, developed by the researcher, allowed for the control of confounding variables that may have affected the study as well as the collection of demographic information. Information was collected regarding the children's home language, the language of education, the attendance at preschool, the type of school, the parent's level of education, the parent's occupation and

living amenities, as these have all been shown to influence cognitive development (Tinajero & Loizillon, 2010). Furthermore the child's name, gender, date of birth, medical evaluations (CD4 count and viral loads) and HAART information was also indicated on the demographic questionnaire. (Refer to demographic questionnaire in Appendix A)

Although it was assumed that the participants used in the study were from a similar Socio-economic status (SES) due to the lack of private medical insurance and their attendance at the governmentally-funded hospital where the study took place, the researcher collected information regarding the socioeconomic status of each child. This information was collected through the use of the Living Standards Measure (LSM) in the demographic questionnaire. The LSM was created by SAARF and has become the most widely used tool to segment the population of South Africa across race, age, gender or any other variable used to categorise people. This measure groups people according to their living standards (Eighty20, 2008).

Automated Working Memory Assessment (AWMA, Alloway, 2007). This computer-based measure is used to assess working memory profiles from early childhood (4 years) to adulthood (22 years) (Alloway, 2007) and is a standardized tool for non-specialist assessors to screen for working memory impairments in children in order to support and improve learning (Alloway, 2009). Furthermore this measure is a valuable assessment for atypical populations such as those with HIV (Alloway, 2009). The computerized nature of this instrument allowed for the reduction in experimental error and consistent presentation of stimuli and scoring of results across participants (Alloway, Gathercole, Kirkwood, & Elliot, 2008).

This test has not been standardized on a South African population and for this reason a control group of children with similar demographics were used as a comparative group to the HIV positive group. The researcher administered all 12 sub-tests measuring verbal short-term memory (Digit Recall, Word Recall and Non-Word Recall), verbal working memory (Listening Recall, Counting Recall and Backwards Digit Recall), visuo-spatial short-term memory (Dot Matrix, Mazes Memory and Block Recall) and visuo-spatial working memory (Odd-One-Out, Mr. X and Spatial Span) (Alloway, Gathercole, & Pickering, 2004; 2006).

According to Baddeley and Hitch's (1974) working memory model, the verbal short term tasks associated with the phonological loop were the Digit Recall, Word Recall and Non-word Recall. In Digit Recall, participants were asked to repeat to the number that is heard from the computer. In Word Recall the participants were asked to repeat each one-syllable

word they heard from the computer and Non-word Recall the same process was followed but the one-syllable words were unrecognizable to the participant as they do not exist in the English language (Alloway, 2007). The participants were asked to repeat the words or numbers in the exact sequence. The verbal working memory measures, these included the Listening Recall task, the Backward Digit Recall and the Counting Recall. All verbal working memory tasks were associated with the central executive aspect of Baddeley and Hitch's working memory theory (Alloway, 2007). The Listening Recall required the participant to listen to series of spoken sentences and then required to identify whether the sentence was "true" or "false" as well as recall the last word of the sentence, engaging the working memory functioning. The Backwards Digit Recall test compelled the participant to listen to a series of digits and then recall then in the reverse sequence. The Counting Recall task required the participant to count a series of red circles in screen filled with red and blue triangles are circles. Following which the participant must recall the total amount of red circles after he/she has counted them and continue to do so through the varying levels (Alloway, 2007).

The short-term visuo-spatial aspect of working memory was assessed by the Dot Matrix, the Mazes Memory task and the Block Recall task. In the Dot Matrix the participants were shown 4 x 4 matrices on the screen where a red dot appeared and the participant must recall the position of this dot by pointing out where the dot was after it has disappeared to the examiner on the computer screen. In the Mazes Memory task, the participants were presented with a maze and were instructed to trace the path for the stick figure to get out of the maze. The Block Recall test, the participants were presented with a video of various blocked being tapped and then they were asked to mimic this video. (Alloway, 2007). Finally, three measures in the AWMA were associated with the visuo-spatial working memory aspect of Baddeley and Hitch's working memory model which is the central executive and these were the Odd-One-Out test, Mr. X and Spatial Recall. In the Odd-One-Out test, the participants were presented with three shapes and asked to identify the shape that is the odd-one-out and then recall which block out of the three empty blocks it was in. in the Mr. X task, the participant was presented with 2 Mr. X figures. They then were instructed to identify whether the Mr. X with the blue hat was holding the ball in the same hand as the Mr. X with the yellow hat. To further complicate this task, the Mr. X with the blue hat is rotated and the participant is also asked to recall the position of the ball on a picture with eight compass points. (Alloway, 2007). Lastly, the Spatial Recall test required the participants to view two

shapes. The one on the right had a red dot on top and the participants were asked to identify if the shapes were the same or not. The shape with the red dot was rotated and then as with the Mr. X test, the participants were also asked to recall were the red dot was by indicating on the eight compass point picture (Alloway, 2007). The 12 AWMA tests are randomly mixed up so as to provide a variety and break for the participant's short-term and working memory.

The AWMA subtests are presented in fixed sequence on the computer so as to reduce fatigue and vary task demands (Alloway, Gathercole, & Pickering, 2006). The test was presented to participants on a laptop computer and was designed using Borland's C + + Builder 5 (Alloway, Gathercole, & Pickering, 2004). The instructions in the AWMA were presented as an audio with a blank white screen which is followed by practice items for each sub-test. The processing and storage tests (working memory tests) were presented individually in the practice rounds as well as a combined task (Alloway, Gathercole, & Pickering, 2006). Each test trial consisted of 6 rounds and if the participant received four correct results it automatically moved up to the next level. The researcher scored the responses on the laptop keyboard: a correct response with the right arrow key, the incorrect response with the left arrow key and to move either up or down a level the up and down arrows are used respectively (Alloway, Gathercole, & Pickering, 2006). The discontinuation rule for each test is three or more incorrect responses. The program then exited that sub-test and automatically generate the standardised scores (mean = 100, SD = 15) for that memory sub-test (Alloway, Gathercole, & Pickering, 2006; Alloway, Gathercole, Kirkwood, & Elliot, 2009).

As for validity, the AWMA has convergent validity with the WISC-IV Working Memory Index with scores ranging from <86 to >95 among children (Alloway, 2007a). Furthermore divergent validity was found when the AWMA was compared to the Working Memory Rating Scale. The AWMA was found to focus more on cognitive aspects of working memory whereas the WMRS was found to measure more behavioural characteristics of working memory (Alloway, 2007a). The test reliability of the AWMA; the instrument was tested on 128 individuals randomly selected across schools as well as universities ranging from 4 years old to 22 years old. Over a four week period, a close relationship was identified between the two tests indicating a very small change between the results. These results ranged from .69 to .90 which indicates a moderate to high reliability which is important for a large scale test like the AWMA (Alloway, 2007).

Raven's Coloured Progressive Matrices (RCPM, Raven, 2000). This test was included in the instruments as a measure of non-verbal intellectual ability to determine whether the groups were compatible in this regard and furthermore it is known to be correlated with working memory performance (Conway, Cowan, Bunting, Therriault, & Minkoff, 2002; Raven, 2000). It allowed the researcher to control for cognitive functioning differences across the different groups (Raven, Raven & Court, 1998). The RCPM is a visual modality test of reasoning that creates an intelligence score based on a regression equation. Furthermore this test of general intelligence is seen as "culture-free" owing to its non-verbal format (Dawes & Grant, 2007). The test required each child to complete a geometric figure by choosing one of the six choices to fill in the missing segment (Engle, Santos, & Gathercole, 2008). The parts are simple shapes that with only one correct answer among a series of similar shapes (Martin & Weichers, 1954). The instrument has 36 items divided into twelve series and was scored for each correct answer therefore allowing for a maximum score of 36 (Martin & Weichers, 1954). The matrix designs are colourful so as to attract the child and each item is presented on an individual page (Martin & Weichers, 1954). Furthermore according to Martin and Weichers (1954), the Coloured Progressive Matrices have more extensive use in the clinical testing of children contributing to the rationale of its use in these samples.

With regards to validity and reliability, a study comparing the RCPM and the WISC tests show correlations of .91 between the full scale, .84 for verbal IQ's and .83 for performance IQ's (Martin & Weichers, 1954). The retest reliability across development was found to be .90 which shows that this test is reliable measure of general cognitive functioning (Raven, Court & Raven, 1990). Considering this study was investigating ages 6 to 8; a study conducted by Carlson and Jensen (1981) revealed split-half reliability estimates of .65, .86 and .85 for those specific ages, indicating a consistent measure of cognitive ability for the samples that will be used in the following study.

Sentence Repetition Test (SRT) (Redmond, 2005). This instrument measured English language proficiency. The measure consists of sixteen 10 word sentences divided equally into active and passive tense. It requires the child to repeat the sentence read to them by the researcher and the test is then scored as follows: 2 (correct), 1 (three or fewer errors) and 0 (more than 4 errors), allowing for a maximum score of 32. Furthermore this measure was developed to be a particular length to allow for normally developing children to make enough errors that would allow for group comparisons to be conducted. An inter-rater reliability measure of .95 was calculated for this specific recall probe (Redmond, 2005). This instrument

works off a concept referred to as elicited imitation which requires a participant to imitate a series of sentences to a person through repetition. This is effective in English additional learners because should English be unknown to the participant, then they are required to hold the sentence in working memory and imitate it back to the researcher, indicating that working memory and second-language ability are not independent of one another (Okura & Lonsdale, 2012). Thus to rule out language proficiency in the interaction between the HI virus on working memory, this measure needs to be assessed and controlled for.

Procedure

The HIV positive group and the control group were recruited in a non-probability, convenience sampling manner. The HIV positive participants were sourced from one of the University of the Witwatersrand's government teaching hospitals. The healthy control group was sourced from the Paediatric Out Patient Department (OPD) (dental clinic and general OPD clinics) of the teaching hospitals. Additionally, the hospitals selected for data collection ran aggressive Voluntary Counseling and Testing (VCT) of all patients regardless of their reason for the visit which includes a pre-testing session and post-testing session where the patients are given information about the HIV and encouraged to engage in positive behavior change.

The head of the hospital's research units gave verbal permission for this study to be conducted. Ethical clearance from the University's medical research committee had already been obtained as this study is an extension of a larger study investigating working memory profiles in HIV infected, HIV exposed uninfected children. (See Appendix E).

The researcher, with the aid of staff members, approached participants' legal guardians whose children complied with the inclusion and exclusion criteria for groups 1 and 2 whilst they waited for the child's appointment with the doctor. The researcher then introduced herself and gave the legal guardian a description of the research followed by an invitation to allow their child to participate in the study. They were informed that they are in no way forced to participate and that there are no negative effects for declining participation with the researcher and the clinic. If the parent or guardian provided verbal consent for the child's participation, they were presented with an information sheet (see Appendix D), a demographic questionnaire (see Appendix A), an information booklet on working memory

and a written consent form (see Appendix B) that they were instructed to fill out in the waiting room whilst the child was completing the tests with researcher.

If translation was required for the English measures, the parent or legal guardian was asked to be present during testing to assist the researcher in performing the tests by translating the instructions into the child's home language. The caregiver provided information about the type of ARV medication the child was receiving to provide comparable demographic results. Following these steps, the child accompanied the researcher to a specified room in the clinic where the child was read the assent form (see Appendix C) and asked to sign their name and then the three tests were administered. This testing took on average an hour to an hour and a half to complete depending on the cognitive ability of the child. If the child's appointment time with the doctor coincided with the testing, the parent or legal guardian was instructed to interrupt the researcher and the testing was put on hold so as to not disrupt the clinic and their proceedings. Upon completion of the three instruments the child was served light refreshments and if the parent has specifically arrived for the participation in the research and not the appointment, they received a small stipend to cover transport costs. Finally brief, verbal feedback was given to parents/guardians who requested it.

Ethical Considerations

Ethically there are a number of aspects that needed to be considered due to the sensitivity of the samples used. The HIV sample is a difficult population due to the complex nature surrounding the status of each participant. This study was a part of a larger study for which ethical clearance had already been obtained. (See appendix E for the ethics clearance certificate.)

The researcher assumed that the population attending the clinic was HIV positive as they attended the clinic to have quarterly medical check-ups and to replenish their HAART medication and thus satisfied the inclusion criteria for the study. The researcher then identified possible candidates with the help of the nurses and staff at the clinic that were within the age range. Following this, the researcher asked to speak to the parent or legal guardian privately and confidentially. She then informed them about the study and how data would be collected. The researcher explained that there were no negative effects for declining participation in the study. If the parent or legal guardian provided informed verbal consent, he/she was presented with an information sheet for the study, an information sheet on working memory and working memory exercises, demographic questionnaire and the written

consent form. The researcher then explained to the parent or legal guardian that he/she may remain in the queue for the doctor in the waiting room whilst completing the demographic questionnaire and when it is time to see the doctor he/she may remove the child from the tests so that they were in no way negatively affected by the participation.

Patient anonymity was not possible as the researcher needed to interact with child and the parent or guardian, as well as have access to the child's medical file for the information regarding their HIV status and HAART information. Once captured, the information was treated confidentially and was anonymised by assigning a code to each participant. If the possible candidate was not able to conduct the testing on the day that they have an appointment, a stipend of R150 was offered to the participants to cover transportation costs of returning on a separate day that suited both the researcher and the candidate. Lastly, if the participant performed particularly poorly on any of the tests conducted, they were referred to the Psychology Department, the Speech and Audiology Department or the hospital's resident Child Psychiatrist for further assessment.

Data Analysis

The study was non-experimental and therefore causality between the variables cannot be inferred. The study's primary aim was to compare working memory function between the two samples. The statistical analysis program IBM SPSS statistics version 20 was used to analyse the raw data (IBM Corporation, 2012).

The data provided was interval in scale, the sample was random and independent, there was equality of variance and the histograms provided normal bell curves, thus parametric tests were conducted. Descriptive statistics summarised means, standard deviations, ranges, normality and other measures of skewedness of the dependent variables. The reliability for the subtests of the AWMA could not be calculated as the computer-based program does not supply individual scores but rather an overall score for each subtest.

Once the above statistics were conducted and assumptions met; Independent-tests determined whether the two groups differed significantly on the SRT and the RCPM. Correlation analyses were conducted between the covariates and the dependent variable, working memory. Multivariate Analyses of Covariance (MANCOVA's) compared the dependent variables between the two groups, with SRT and RCPM as covariates.

Chapter 3

Results

In order to address the research questions, a series of statistical analyses were conducted on the data collected. Firstly, analyses assessing the suitability of the data for parametric analysis were conducted, followed by analyses describing the data. These pre-analyses were followed by a number of statistical tests that assisted the researcher in addressing the research questions, which focused on comparing the working memory profiles of HIV affected and unaffected children.

Normality of the data

According to Howell (1997), five assumptions need to be met before parametric techniques are applied. These include random sampling and independent sampling which assumes that each person in the population has an equal yet random chance of being selected for the sample. This was assumed for the above sample. Thirdly, normality was tested by inspecting histograms seen in appendices F, G and H.

The dependent variables of the working memory measures, the non-verbal intellectual ability measure and the language proficiency measure are all at least interval scaled measures, indicating the fourth assumption of interval scaled measures has been met. Equality of variances is the final assumption and needed to be met when the t-test analyses were completed between the two groups. The Levene's tests for equality of variances were not significant for SRT: $F = .188$, $p = .667$; RCPM: $F = 1.442$, $p = .235$; Digit Recall: $F = 1,48$, $p = .22$; Listening Recall: $F = .54$, $p = .47$; Counting Recall: $F = .08$, $p = .77$; Backwards Digit Recall: $F = .01$, $p = .93$; VWM_scaled: $F = .95$, $p = .34$; Dot Matrix*:* $F = .08$, $p = .80$; Mazes Memory: $F = .24$, $p = .62$; Block Recall: $F = 1.17$, $p = .29$; VSSTM_scaled: $F = 1.33$, $p = .25$; Odd-One-Out: $F = .14$, $p = .71$; Mr. X: $F = .06$, $p = .34$; Spatial Recall: $F = .93$, $p = .34$; VSWM_scaled: $F = 1.00$, $p = .32$. They were significant for Word Recall: $F = 4.59$, $p = .04$; Non-Word Recall: $F = 4.96$, $p = .03$; VSTM_scaled: $F = 4.78$, $p = .03$. The majority were not significant, indicating that there is equality of variance and the assumptions have been met. Therefore normal parametric analyses were conducted.

Descriptive statistics

The descriptive statistics for the working memory measures and the two covariates of non-verbal IQ and language proficiency can be seen in Table 2 below.

Table 2

Means and Standard Deviations of the Two Groups for All Measures

		HIV-positive (n = 26)		Control (n = 26)	
		Mean	SD	Mean	SD
SRT		7.23	6.89	18.08	7.77
RCPM		11.96	4.16	19.62	5.63
Simple Verbal	Digit Recall	20.08	3.92	23.73	5.01
WM	Word Recall	13.92	4.82	16.88	3.66
	Non-word Recall	12.85	4.32	12.96	2.78
Complex	Listening Recall	2.12	3.18	5.23	4.47
Verbal WM	Counting Recall	9.12	3.23	10.08	3.73
	Backwards Digit Recall	3.69	2.78	8.35	3.86
Simple Visuo-spatial WM	Dot Matrix	12.88	3.53	13.73	2.49
	Mazes Memory	10.69	4.66	10.15	5.70
	Block Recall	13.04	2.49	12.42	2.90
Complex	Odd-One-Out	9.08	4.54	13.62	4.35
Visuo-spatial	Mr. X	4.73	3.17	5.04	2.81
WM	Spatial Recall	7.19	5.01	8.50	3.63

Notes. RPCM = Raven's Coloured Progressive Matrices; SRT = Sentence Repetition Test ; WM = working memory

Non-verbal ability

Since research indicates that nonverbal intelligence and working memory are separate but highly correlated constructs, as both involve the use of the prefrontal cortex, it was necessary to first compare the groups on the RCPM (non-verbal IQ) (Conway, Kane, & Engle, 2003). Through an independent samples t-test, a significant difference ($t(50) = 5.58$, $p = .000$) was identified. As seen in Table 2, the means reveal that the control group performed significantly better than the HIV group. Thus, RCPM was entered as a covariate in comparisons between the groups.

Language Proficiency

Secondly, language proficiency was assessed as participants' home language was not English. They were all assessed in English, and thus the effects of this needed to be controlled for. Therefore, an independent samples t-test was conducted on language

proficiency (SRT) between the two groups. A significant result was identified ($F(50) = 5.33$, $p = .000$) indicating that language proficiency differed significantly between the groups, with the control group performing better than the HIV group. Thus, the language proficiency test was entered as a covariate in comparisons between the two groups.

Correlation Analyses

Pearson's correlations were conducted to see whether there was a relationship between the covariates, language proficiency and non-verbal IQ and the dependent variable working memory. These can be seen below on table 3.

Table 3

Pearson's correlations between the components of the working memory and the covariates, language proficiency and non-verbal ability

	SRT		RCPM	
	HIV +	Control	HIV +	Control
Verbal STM	.19	.10	.02	-.01
Verbal WM	.47*	.39	.21	.16
Visuo-spatial STM	.19	-.17	.28	.31
Visuo-spatial WM	.35	-.15	.37	.05

Notes. STM = short-term memory; WM = working memory; * p < .05; SRT = Sentence Repetition Test; RCPM = Raven's Coloured Progressive Matrices

A significant positive correlation was found between language proficiency and verbal working memory. This indicates that there is a correlation among the variables and thus must be treated further as covariates to working memory.

Working memory

Since non-verbal intelligence and language proficiency were significantly different between the groups, a series of Multivariate Analyses of Covariance (MANCOVA's) were conducted with these variables as covariates where alpha was set at p < .05. In terms of the verbal aspect of Baddeley's Multicomponent working memory model, verbal short-term memory, the Digit Recall, Word Recall and Non-word Recall tests were all investigated with no significant differences identified in the first MANCOVA with non-verbal ability and language proficiency as the covariates (Table 4).

Thus, there is no significant difference between the verbal short-term memory functioning in the HIV group and the control group. When investigating verbal working memory there were

no significant differences between the groups on the Listening Recall task, the Counting Recall task and the Backwards Digit Recall task, although the difference between the groups on Counting Recall was approaching significance.

Table 4

Multivariate Analyses of covariance (MANCOVA) between groups on all working memory measures

		df	*F*	*p*	*d*
	Digit Recall	1	.04	.85	.81
	Word Recall	1	.01	.93	.69
	Non-word Recall	1	.00	.96	.03
Total	Verbal STM	1	2.22	.14	
	Listening Recall	1	.10	.75	.80
	Counting Recall	1	3.87	.06	.28
	Backwards Digit Recall	1	3.12	.08	1.39
Total	Verbal WM	1	2.63	.11	
	Dot Matrix	1	1.80	.19	.28
	Mazes Memory	1	13.70**	.00	.10
	Block Recall	1	4.13*	.05	.23
Total	Visuo-spatial STM	1	.68	.42	
	Odd-One-Out	1	.33	.57	1.02
	Mr. X	1	1.57	.22	.10
	Spatial Recall	1	.92	.34	.30
Total	Visuo-spatial WM	1	.65	.42	

Notes. STM = short-term memory; WM = working memory; * $p <$. 05; ** $p <$ .001

Visuo-spatial short-term memory was investigated through the Dot Matrix, the Mazes Memory and the Block Recall tests. The MANCOVA revealed significant differences between the groups on the latter two tests. (Refer to Table 4). However, the effect sizes for these suggest that the practical significance is small.

The MANCOVA conducted for the visuo-spatial working memory tasks revealed no significant differences between the groups on the Odd-One-Out, Mr. X and Spatial Recall tasks. Lastly the MANCOVA results for the overall scaled values for all four components (namely verbal STM, visuo-spatial STM, verbal WM and visuo-spatial WM) of the model are given for both groups in Table 4. All components showed non-significant results indicating there is no difference in working memory or short-term memory between the HIV group and the control group but too subtests comprising the visuo-spatial short-term memory score were

significantly difference and so this total score masks these differences. This could be a result of a number of confounding factors and limitations that were met during this study. The following discussion will address and explore the results above. The discussion section elaborates on these results, with reference to the theory and previous research.

Chapter 4

Discussion

This research investigated the HI virus and working memory in South African children when compared to controls. In doing so, the study adds to the relatively sparse knowledge base regarding the neurocognitive effects of HIV in a developing country such as South Africa where the prevalence of HIV is so high (Msellati, Lepage, Hitimana, Van Goethem, Van de Perre, & Dabiis, 1993). Together with the multitude of negative effects this virus has on a person, one of the most serious consequences is the impact on the central nervous system (CNS) and thus neurocognitive deficits are anticipated (Pumariega, Shugart, & Pumagiera, 2006). Through the use of the Automated Working Memory Assessment (AWMA), the working memory profiles of 26 HIV positive and 26 HIV negative children were compared. Language proficiency and non-verbal intelligence were also investigated and treated as covariates in this study as both variables are known to share a relationship with working memory (Conway, Kane, & Engle, 2003; Kane & Engle, 2002; Okura & Lonsdale, 2012).

Although Alloway et al., (2009) discovered that is better to investigate working memory deficits through domain-general components like the central executive rather than the domain-specific visuo-spatial sketchpad and the phonological loop, for the purpose of this study, all four aspects of the multicomponent model were assessed in order for a full working memory profile to be defined for HIV positive children and compared to that of a control. When the four components of Baddeley and Hitch's model were analysed, no statistically significant differences were found between the HIV positive and the control group because the sum of the subtest scores were not strong enough to reach significance for the total components. However, the differences that were found were on the Block Recall and the Mazes Memory subtest. The Block Recall and the Mazes Memory subtests both measured the visuo-spatial short-term memory in this population. This implies that the HI virus did not affect the specific components of working memory of the chosen population but rather specific subtests in the visuo-spatial aspect of short-term memory. This is not consistent with previous work conducted by Martin et al. (1999) who discovered a diffuse deficit in HIV across all types of information and types of working memory processes rather than specific verbal or visuo-spatial aspects and reasons for this inconsistency could be attributed to the differences in the sample as the Martin et al. (1999) study used an adult population with the mean age of 44.1 years for the HIV positive group and 45.8 years for the matched control

group whereas this study used a middle childhood sample. Furthermore, the Martin et al. (1999) study only used males and the current study utilised a mixed gender sample. In the current study, the statistical analyses revealed no significant differences between the groups on the verbal short-term memory tasks.

What this means is that the HI virus appears not to have affected this aspect of memory in the population under investigation. Since short-term memory is a simple rapid-access, input-and-retrieval system, it is less likely to be affected by HIV than other higher executive functions, although this was not the case in the current study (Zillmer, Spiers, & Culbertson, 2008). The reason for significant differences being found in the visuo-spatial short-term memory and not in the verbal short-term memory can be attributed to certain sub-cortical brain areas being affected more so than others. Verbal working memory was also investigated and the statistical results showed no difference between the HIV positive and HIV-negative group. All the results mentioned above for verbal short-term memory and working memory in children are consistent with the literature that indicates a diffuse deficit in the working memory of adult and child patients with HIV/AIDS rather than specific deficits (Angelini et al., 2000; Fishkin et al., 2000; Martin et al., 1999). The AWMA also assessed the working memory tasks associated with the right hemisphere, the visual and spatial aspects. Firstly, the visuo-spatial short-term memory tasks revealed two significant differences between the two groups, on the Mazes Memory task and on the Block Recall task, with the HIV group performing significantly poorer than the matched controls. The visuo-spatial working memory tasks revealed no significant differences between the groups. When comparing these results to existing literature, there is little correlation. This may be attributed to the innovative nature of the study or certain limitations in the execution of the research. Nonetheless, such results are important as it is critical to identify areas of developmental weakness in HIV positive pediatric patients.

The study also investigated two other neurocognitive variables, namely non-verbal intelligence and language proficiency. It was discovered than language proficiency and non-verbal ability are both significantly correlated with verbal working memory when the HIV positive and the matched control group were compared separately. This finding further exemplifies the link between working memory's executive function, language proficiency and HIV as all utilize the prefrontal cortex (Payne & Whitney, 2002). When non-verbal IQ was compared between the HIV group and the control group, a significant difference was discovered in favour of the control group, and similarly for language proficiency.

Consequently, non-verbal IQ and language proficiency were covaried in the comparisons between the two groups. Therefore the current study produced results that are in accordance with the previous studies conducted by Ruel et al. (2011) who found that there were significant cognitive deficits in HIV positive children when compared to healthy controls, van Loon (2009) whose results showed a significant lower cognitive functioning in South African HIV positive children compared to controls (mean age 10.2 years) and Koekkoek et al. (2008) who found the largest impairment in executive functioning in peri-natally HIV-infected children compared to matched controls.

Gevin and Smith (2000), who assessed 80 healthy young adults (mean age 21.4 years) assessing the relation between verbal and non-verbal working memory and general cognitive ability, found that participants with a higher general intelligence ability made relatively greater use of the parietal regions of the brain whereas participants with lower general intelligence ability made greater use of frontal regions. It is possible that the children in the current study were employing similar brain areas, because the link between general intellectual ability resulted in the HIV positive group having a general lower IQ than their matched controls and thus placed a larger emphasis on the frontal lobes rather than the parietal lobes. As research proves, the frontal lobe controls the higher order functioning and thus implies the virus places a greater pressure on the frontal lobes as the virus attacks it. Furthermore the pattern of performance for the subjects in Gevin and Smith's (2000) study varied substantially from each other. Patients with high-ability confronted the visuo-spatial working memory tasks using their dorso-lateral prefrontal cortex, implicated in executive functioning; but as the patients formulated an effective task strategy, parietal regions were activated for more domain-specific functioning.

In Gevin and Smith's (2000) study, the opposite pattern was noted for the low-ability patients, domain-specific region were activated initially followed by limited capacity frontal lobe regions when organizing information from working memory tasks (Gevin & Smith, 2000). This study can be related to and used to support the current study's findings, as the children with HIV who showed low general cognitive ability on the Raven's Progressive Colour Matrices revealed less executive function control in the working memory task, suggesting that the prefrontal cortex may have been affected by the virus, in comparison, to the control group who scored significantly higher on the non-verbal ability task. Although this data is inferred, the specific brain systems activated in this study could not be recorded as

it was beyond the scope of this study, thus further research may focus on the brain areas activated in HIV patients on the tasks utilised in this study.

Reasons for the specific effects on two subtests found in this study could be attributed to a number of limitations of the study, as well as other confounding factors that could not be controlled for. Firstly, the study was conducted in South Africa, a developing country where the majority of the population (62%) is living under the poverty line (AdvocacyAid, 2013). This issue of poverty affects the child's ability to receive the appropriate education and stimulation needed to develop their working memory. Thus, even though the age group chosen for this study is considered to have a functioning working memory and the reliance on the visuo-spatial short-term memory is strongest at this age; the children included in this study's sample may not have functioning working memories due to a number of confounding factors such as nutrition, upbringing, preschool attendance, interaction and stimulation with people and objects, etc. (Gathercole, Pickering, Ambridge, & Wearing, 2004; Grantham-McGregor, Cheung, Cueto, Glewwe, Richter, & Strupp, 2007; Siegel & Ryan, 1989). The confounding factors resulting from poverty are many and exceed the scope of this research report. Therefore the researcher proposes further research that attempts to control for more confounding factors as a result of poverty.

As indicated earlier, one of the critiques of Baddeley and Hitch's (1974) theoretical model is that the visuo-spatial sketchpad seems to be more fractionated than initially theorized. Furthermore, more investigation into the nature of rehearsal in the sketchpad as well as the precise nature of this subsystem still remaining unclear and could account the two visuo-spatial short-term memory subtests being significant (Baddeley, 2012). Additionally, the relatively small sample size is an unfortunate disadvantage to the current study. The low numbers included in each group can be contributed to the length of the instruments and the number of confounding factors the researcher was introduced to during data collection. The clinics chosen were only open for four hours twice a week and each test took approximately an hour and a half to complete. Therefore only a few participants could be tested each day. Secondly, the number of children in the age range who attended the clinic on the chosen data collection days depended solely on the register at the clinic and thus was out of the control of the researcher. Thirdly, the POPD where the control group was sourced from was difficult to recruit participants as the age range was difficult to find on each given day. Therefore, a number of limitations affected the sample size and account for this disadvantage.

Lastly, the study included patients from an HIV clinic in South Africa. According to Ruel et al. (2011) patients with extremely high CD4 counts are ineligible for HAART medication. This is the group that is essential to study as the advanced effects of HIV on the developing brain will be highly apparent in these children. But the clinics do not give ARV's to this group of children and with the advancements in testing, a large percentage of school-going children are now being diagnosed HIV-positive. This causes a problem in research as the children who need the interventions and help cannot receive it due to their high CD4 count. This problem may account for the lack of significant results in the main research questions for this study as the HIV participants tested were all on HAART and thus have significantly lower CD4 counts, so that the effects of the virus would be less noticeable in this sample. In order to fully investigate the effects of HIV on working memory in children, it would be necessary to conduct a study on a sample with extremely high CD4 counts that are ineligible for the HAART.

The results of the current study suggest is that the impact of the HI virus on working memory in middle childhood in a South African population is not generally significant other than visuo-spatial short-term memory but rather overall neurocognitive dysfunction in aspects such as language proficiency and non-verbal intelligence are apparent. These results are further supported by the studies conducted by Ruel et al. (2011) in Africa and van Loon (2009) in South Africa who both conducted their studies on children. Ruel et al. (2011) found that there were significant cognitive deficits in visual reaction times, sequential processing, simultaneous processing, planning/reasoning, global performance in HIV positive children when compared to healthy controls and van Loon (2009) found significantly lower cognitive functioning in mental development measured against intellectual maturity in children with the mean age of 10.2 years in the HIV positive group when compared to the control.

Furthermore, this study showed similar limitations to those seen in these two existing studies and thus the interpretation and generalisation of these results is affected as it was in the above research. What these results suggest is that, as seen in Kane and Engle's (2002) and Okura and Lonsdale's (2012) studies, although there is a relation between working memory capacity, non-verbal intelligence and language proficiency in children infected with HIV, this does not seem to result in impaired working memory functioning in school beginners with the exception of visuo-spatial short-term memory which is important for early numeracy (Kyttälä, Aunio, Lehto, Van Luit & Hautamaki, 2003). It seems that the HI virus may have a diffuse effect throughout the brain thus affecting the cognitive neurodevelopment more

generally, including advanced cognitive functions such as language proficiency and non-verbal intelligence in children. These diffuse effects to the brain and CNS are seen in children with HIV in South Africa and affect largely the prefrontal cortex which is implicated in non-verbal ability, language proficiency and aspects of working memory. The diffuse effect the virus has on the child's brain is seen in executive control dysfunction in the prefrontal cortex and specific working memory deficits in other brain regions implicated in visuo-spatial short-term memory. As discussed above, during early childhood visuo-spatial working memory tends to be better developed than verbal working memory (Gathercole & Pickering, 2000).

Future research

With the advances in clinical practice and research, this terminal disease is changing into one that can be controlled and monitored on a long-term basis therefore the need to understand the neurodevelopmental effects is essential (Fishkin et al., 2000). Children infected in HIV can manage this virus through HAART medication. Since working memory is developing from birth through middle childhood, longitudinal studies are needed to focus on the long-term neurocognitive effects this virus has on a child's cognitive development over time. These studies can focus on the differentiation between the cognitive developmental effects of HIV, including poor non-verbal IQ, language proficiency and HIV-PE which develops as a result of the virus, and mental retardation resulting from other factors such as maternal drug addiction or poor pre-natal care as well as specifying the long-term neurocognitive deterioration as a result of the HI virus (Pumariega, Shurgart, & Pumariega, 2006).

Through such studies, health and education professionals can formulate interventions and educational practices that will address the effects of this virus. Through such interventions, counseling can be provided to both the child and their families to facilitate correct educational practices, living conditions and overall healthy environment so that the child can have the best chance at living a long fulfilled life. Furthermore this will potentially cut the educational expenses of the country as early detection of these deficits allows for professionals to rectify them and reduce the need for special education services and the number of children that fall through the gap due to their learning impairments (Fishkin et al., 2000).

Lastly, as mentioned earlier, the children who do not attend the clinics because of their high CD4 counts but have been diagnosed as HIV positive should also be focused on in research. The research that can be done on this population of HIV positive children in South Africa

will extend the knowledge base of how HIV affects the brain neuro-developmentally and more specifically the effects on working memory in advances cases of HIV/AIDS. Every HIV positive child used in this study was undergoing HAART as the form of treatment for HIV at the clinic. The findings suggest that this form of therapy controls the effects that the HI virus has on the child's working memory more generally. HAART is believed to be the most effective form of treatment for HIV. It includes the combination of several antiretroviral drugs that control the amount of virus in the body (Lawn, Badri, & Wood, 2005; U.S. Food and Drug Administration, 2013). The sooner the child is started on HAART, the more beneficial the course of therapy will be. Certain benefits of HAART include a decrease in the severity of early HIV symptoms, a decrease in the rate of disease progress through affecting the rate at which the virus multiplies in the body, preserves the immune system function in the patient, lowers the risk of drug resistance through complete viral suppression and finally reduces the risk of HIV spreading (AIDS, 2009; Healthwise, 2011; Lawn, Badri, & Wood, 2005; U.S. Food and Drug Administration, 2013).

Overall HAART allows the patient to successfully manage HIV and turn the virus from one that is fatal to a chronic lifelong illness (Lawn, Badri, & Wood, 2005). Unfortunately there are risks involved with the use of HAART and these include a high cost of treatment, certain side effects, drug resistance in certain patients, and the need for lifelong adherence to the HAART. This form of therapy is vital to the management of HIV especially in children. The findings of the current study suggest that with correct adherence to HAART, the neurocognitive effects of HIV may be lessened. This finding is extremely important but does require further investigation.

Conclusion

South Africa has the largest number of people infected with HIV/AIDS in the world with 5, 600, 000 people being infected out of 51, 770, 560 (whichcountry.co, 2014). Consequently, effective interventions need to be developed through research so that this can be changed and our country can successfully manage the epidemic (StatsSA, 2013; van Loon, 2009). An unfortunate consequence is the number of children infected with this disease and the effects it has on their neurodevelopment, especially their central nervous system (Brown, Lourie, & Pao, 2000; van Loon, 2009). Long-term outcomes for these HIV-infected children are negative if they are not on HAART, but through research on the neurodevelopment in paediatric HIV, education systems that amend the damage of HIV can be established. This

study produced useful results that show that HIV may have an overall effect on non-verbal ability and language proficiency and a few aspects of working memory such as visuo-spatial short-term memory. The prefrontal cortex seems to be one of the more affected brain areas in HIV positive school-going children in South Africa when compared to controls, largely implicating executive functioning. The current study strengthens results found by Angelini et al. (2000), Koekkoek et al. (2008), van Loon (2009) and Ruel et al. (2011). Further research should focus on addressing the limitations of the current study which include focusing on a larger sample size, developmental longitudinal studies and children with a higher CD4 count who are not receiving HAART. Furthermore, due to the fact that all of the children in the current study were being treated with HAART, this implies that if children with HIV are on HAART and their HIV is effectively managed through this course of treatment, the neurocognitive effects HIV has on the brain are likely to be minimal. This means that according to this study, effects will only be seen in visuo-spatial short-term memory and an early intervention needs to be developed to address this, if it is confirmed with larger sample studies.

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Appendix A: Demographic Questionnaire

Full Name: _____

Home Language: _____ School Language: _____

Gender: M F Date of Birth: D D M M Y Y Y Y

Current Grade: Current School: _____

Has the child started formal schooling (i.e. grade 0)? YES NO

Did the child attend pre-primary school? YES NO

How many years of pre-primary school attended? _____

How many children in the child's class? _____

Does the child attend a school for learners with special needs? YES NO

Are there family members with special needs? YES NO

If so, please provide details:_____

Living Amenities & Caregiving

Who lives with the child? _____

_____

Please indicate the type of place where the child lives

Flat House Shack Shelter Number of bedrooms: _____

Which suburb do you live in? _____

Do you live in a non-urban area? YES NO

Do you live in a house/cluster house/town house? YES NO

Does the child receive a grant? YES NO Monthly Amount:

_____

Do you have

electricity? YES NO

running water? YES NO

flushing toilets inside? YES NO

hot running water? YES NO

A built in kitchen sink? YES NO

domestic workers or gardeners? YES NO

home security service? YES NO

2 cell phones in your household? YES NO

3 or more cell phones in your household? YES NO

a radio set in your house? YES NO

A home air-conditioner? YES NO

TV? YES NO

a swimming pool? YES NO

DVD player/Blu Ray player? YES NO

Refrigerator or combined fridge or freezer? YES NO

Electric stove? YES NO

Microwave oven? YES NO

Deep freezer (free-standing)? YES NO

Washing machine? YES NO

Tumble Dryer? YES NO

Dishwasher? YES NO

A motor car? YES NO

YES NO

Pay TV/DSTV?

A vacuum cleaner? YES NO

Mother

What was the highest school grade passed? _____

Did the mother study after school? YES NO What? _____

Is the mother literate? YES NO

Mother's current occupation: _____

Father

What was the highest school grade passed? _____

Did the father study after school? YES NO What? _____

Is the father literate?

Father's current occupation: _____

Appendix B: Consent form

Psychology
School of Human & Community Development

University of the Witwatersrand
Private Bag 3, WITS, 2050

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

By filling in and signing this document I give permission for my child,

_____ to participate in the study. I understand that I can remove my child from the process at any time without any negative consequences. I allow the researcher to use the data confidentially.

Signed: _____(parent/guardian) Date: _____

Appendix C: Assent form

Psychology
School of Human & Community Development

University of the Witwatersrand
Private Bag 3, WITS, 2050

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

Hello,

My name is (Robyn/Brittany/Fatima), and I am studying at university. I am trying to find out some things about the way children think and learn. I would like to invite you to join me in finding these things out.

If you decide that you would like to be a part of thins, you will need to do three jobs. The first job is a book od coloured puzzles where you need to find the missing puzzle piece. The second one is a job on my computer where we will look and listen to different words and pictures together. The last job is where you and I play copy-cat with 16 English sentences.

It's your choice to do these jobs or not. If you decide that you will do them, you can have as many breaks as you like, and I also have a little snack for you half-way through so you don't get tired. If you decide in the middle of the jobs that you don't want to carry on, that is OK, nothing bad will happen and you will be free to leave the hospital and go home.

Are you happy to help me with my study and do these three jobs with me?

Yes: _____ No: _____

Can you write your name over here?

Researcher's signature in place of child's name if can't yet write their name to indicate verbal consent:

_____

Date: _____

Appendix D: Information Sheet

Psychology
School of Human & Community Development

University of the Witwatersrand
Private Bag 3, WITS, 2050

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

Dear Parent/Guardian,

My name is Robyn/Fatima/Brittany and I conducting research into the effect of HIV and ARV's on the development of children's academic abilities. The research considers the effect of the virus and antiretrovirals on the brain. However, in order to more clearly understand these differences, it is necessary to test uninfected, unexposed children to gain a baseline control for the intention of comparison. Hence, you might have been selected to participate in this research in order to help us understand something that does not directly affect you.

Part of this research requires your responses on the questionnaire below, as well as allowing your child to undergo three brief psychometric tests (The Ravens Coloured Progressive Matrices, the Sentence Repetition Test and The Automated Working Memory Assessment). It should take you approximately 10 minutes to complete the questionnaire, and an hour for your child to finish the testing. I understand that this is a substantial investment of your time. However your response is valuable as it will contribute towards a South African understanding of HIV treatment and will have an impact on research nationally and internationally. I would therefore like to invite you to participate in this research.

Your responses will remain confidential. Should severe academic problems be identified you will be referred to the local psychology department for further assistance, should you wish. You will also receive a small stipend towards your transport money to the

hospital and receive light refreshments during the assessment. Completion and return of the questionnaire will be considered to indicate permission for me to use your responses for the research project. Should you choose not to participate, this will not be held against you in any way. If you have any further questions or require feedback on the progress of the research, feel free to contact me. My contact details appear below my signature.

Thank you for considering taking part in the research project. Please detach and keep this sheet.

Kind Regards,

Robyn Milligan

083 956 1545

milligan.robyn@gmail.com

Appendix E: Ethics clearance

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

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Robyn Milligan

CLEARANCE CERTIFICATE	**M120902**
PROJECT	A Comparison of Working Memory Profiles in HIV Positive and HIV Exposed Uninfected Unexposed Children
INVESTIGATORS	Ms Robyn Milligan.
DEPARTMENT	Department of Psychology
DATE CONSIDERED	28/09/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

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

DATE 24/10/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof Kate Cockcroft

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

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix F: Histograms for Automated Working Memory Assessment for Control group

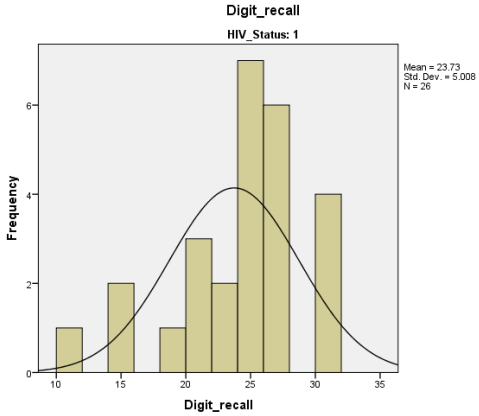


Figure 2. Histogram for Digit Recall for control group

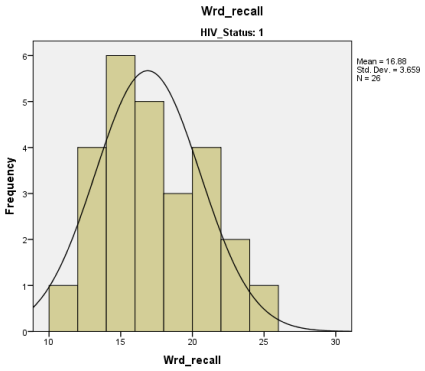


Figure 3. Histogram for Word Recall for control group

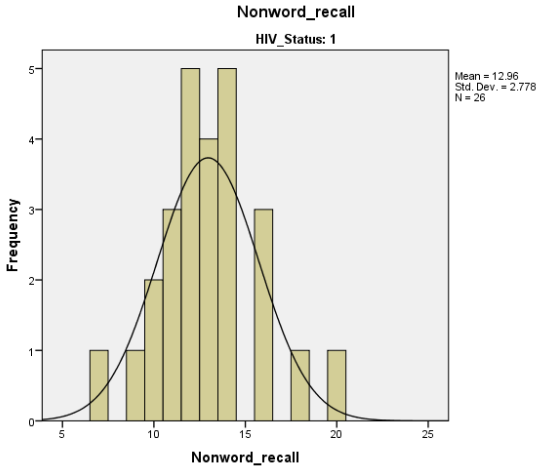


Figure 4. Histogram for Nonword Recall for control group

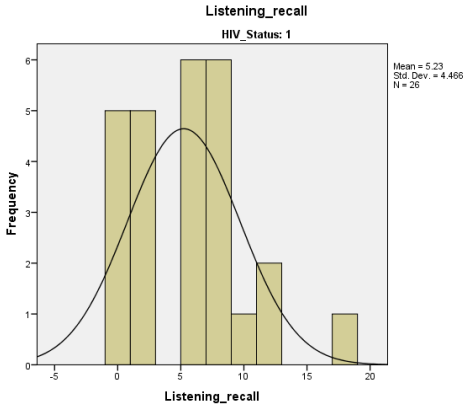


Figure 5. Histogram for Listening Recall for control group

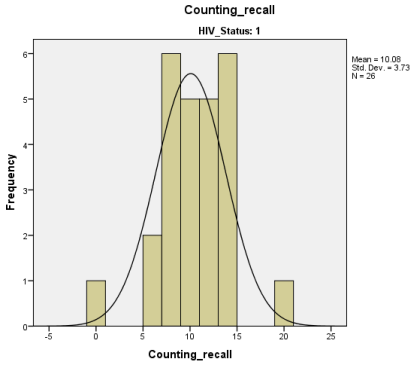


Figure 6. Histogram for Counting Recall for control group

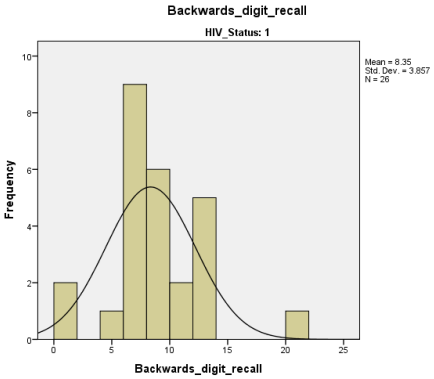


Figure 7. Histogram for Backwards Digit Recall for control group

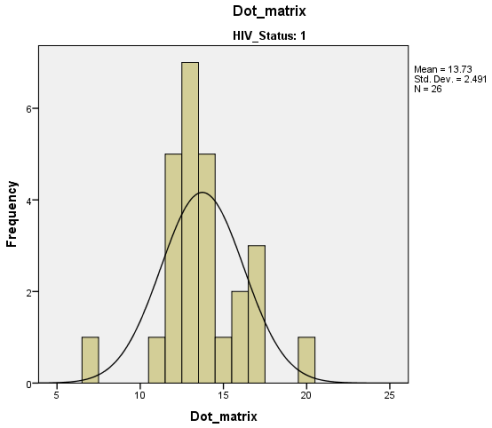


Figure 8. Histogram for Dot Matrix for control group

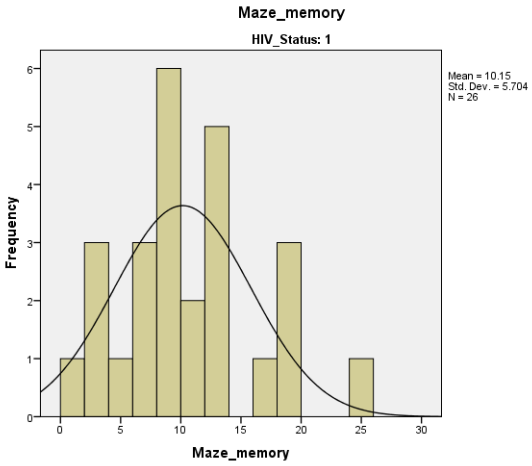


Figure 9. Histogram for Mazes Memory for control group

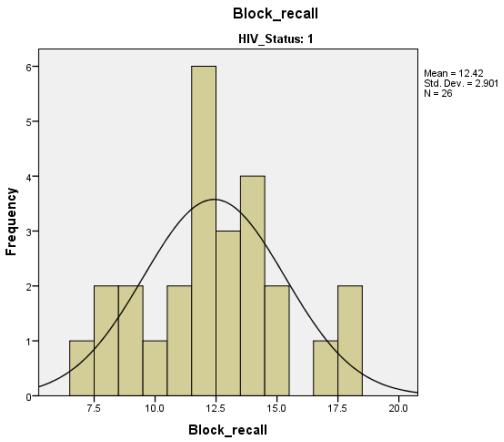


Figure 10. Histogram for Block Recall for control group

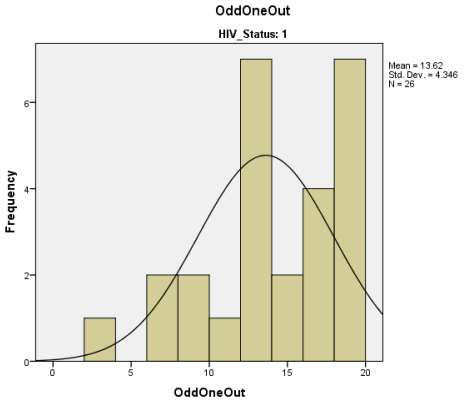


Figure 11. Histogram for Odd One Out for control group

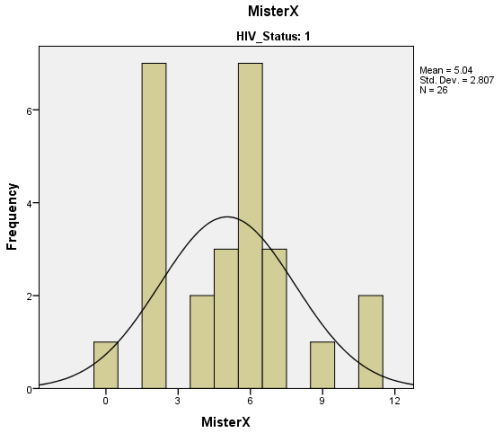


Figure 12. Histogram for Mister X for control group

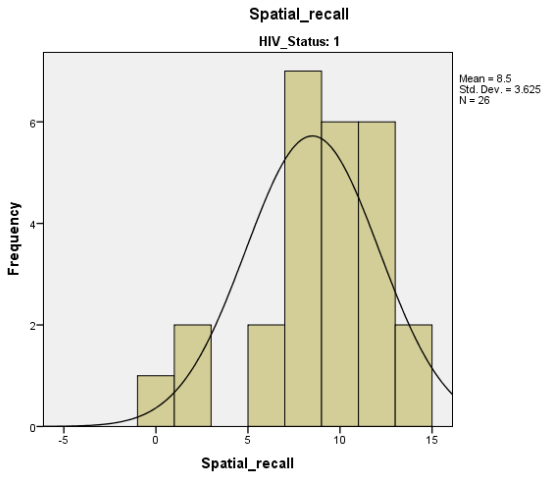


Figure 13. Histogram for Spatial Recall for control group

Appendix G: Histograms for the Automated Working Memory Assessment for the HIV Positive Group

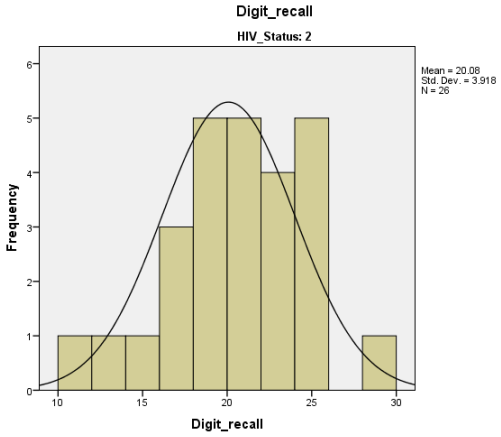


Figure 14. Histogram for Digit Recall for HIV positive group

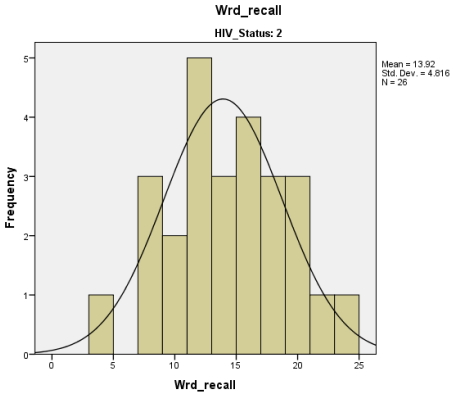


Figure 15. Histogram for Word Recall for HIV positive group

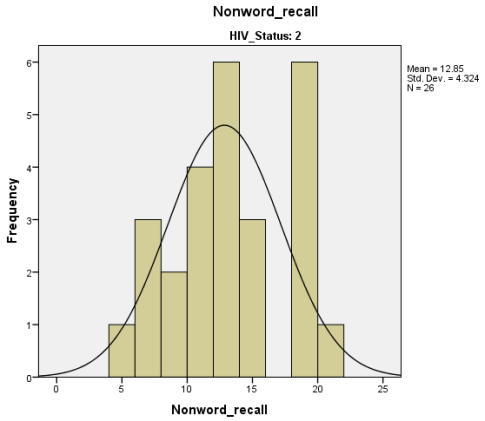


Figure 16. Histogram for Nonword Recall for HIV positive group

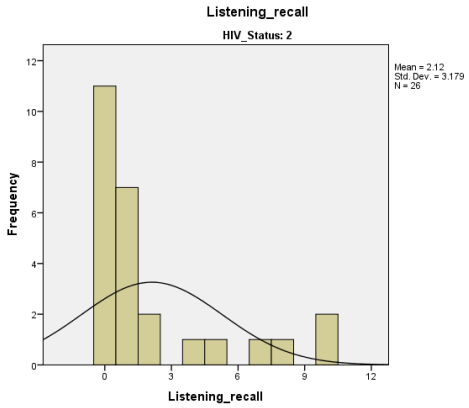


Figure 17. Histogram for Listening Recall for HIV positive group

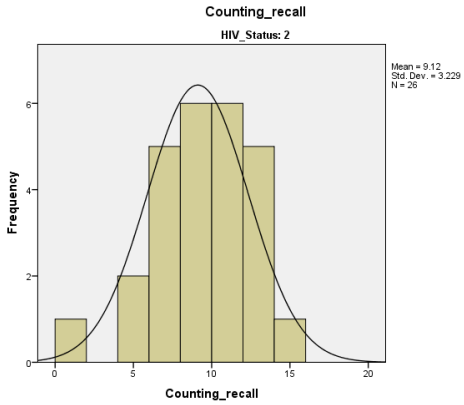


Figure 18. Histogram for Counting Recall for HIV positive group

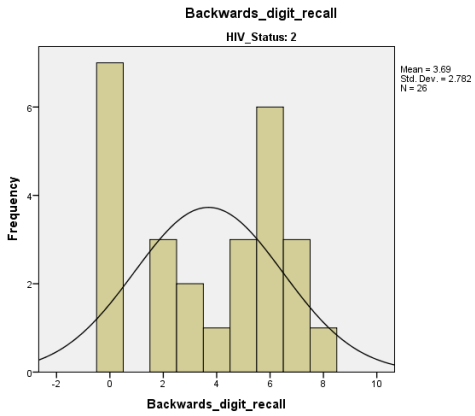


Figure 19. Histogram for Backwards Digit Recall for HIV positive group

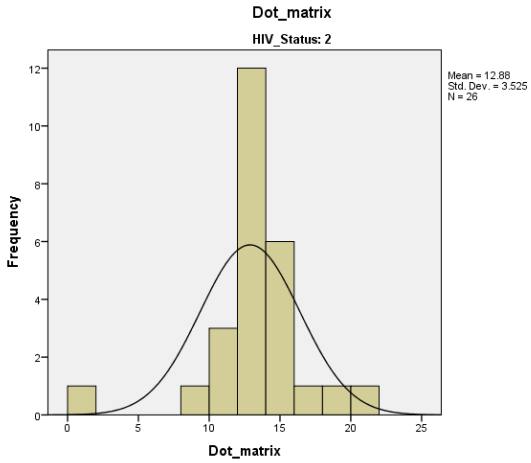


Figure 20. Histogram for Dot Matrix for HIV positive group

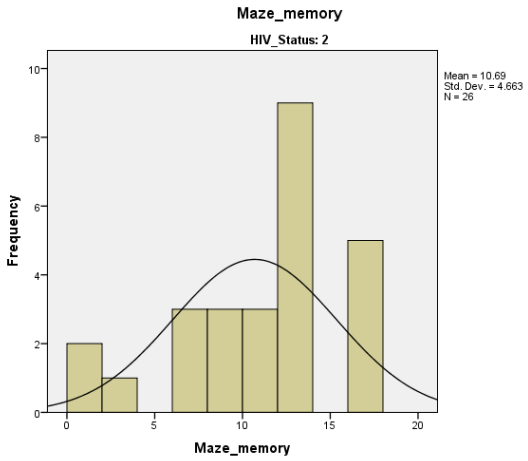


Figure 21. Histogram for Mazes Memory for HIV positive group

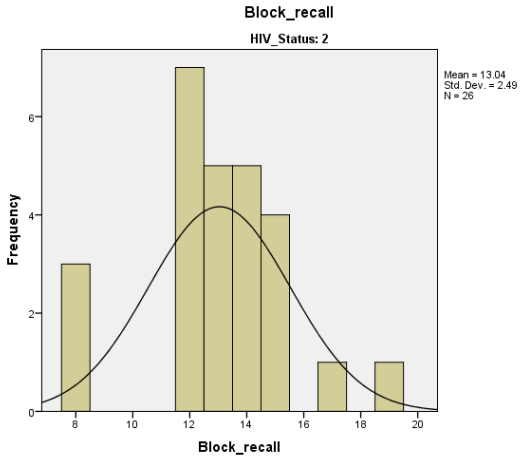


Figure 22. Histogram for Block Recall for HIV positive group

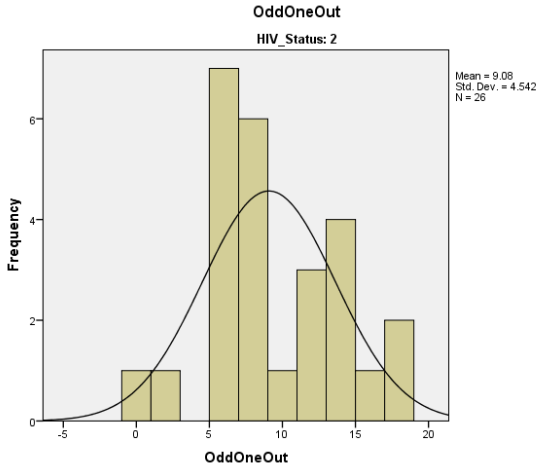


Figure 23. Histogram for Odd One Out for HIV positive group

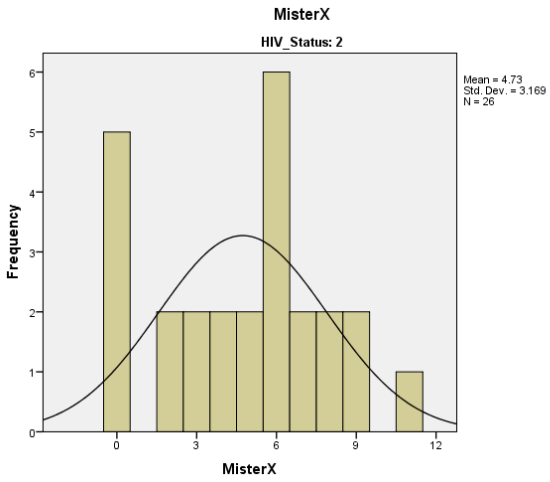


Figure 24. Histogram for Mister X for HIV positive group

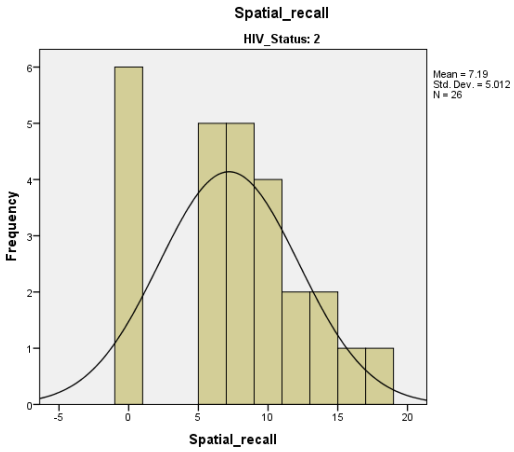


Figure 25. Histogram for Spatial Recall for HIV positive group

Appendix H: Histograms for the Sentence Repetition Test and Raven's Coloured Progressive Matrices for the control group

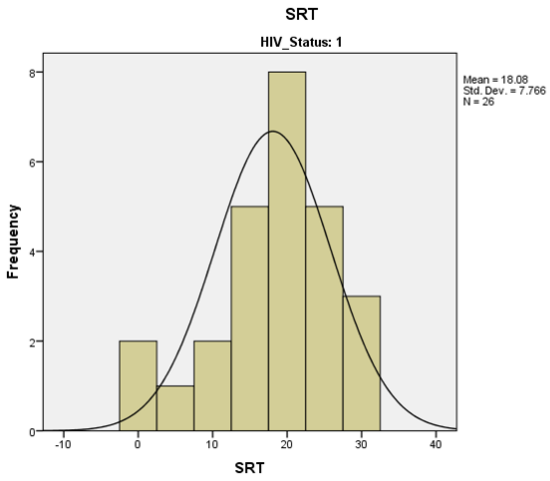


Figure 26. Histogram for Sentence Repetition Test for control group

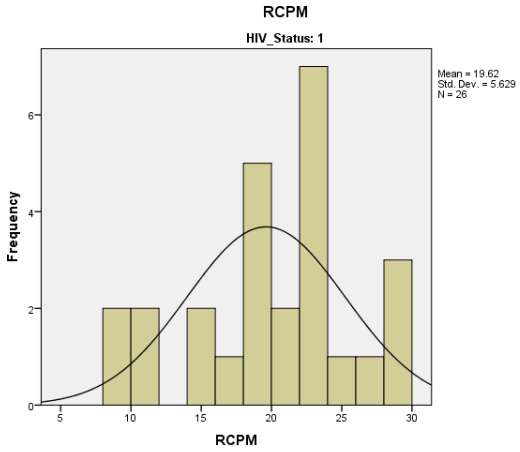


Figure 27. Histogram for Raven's Coloured Progressive Matrices for control group

Appendix I: Histograms for the Sentence Repetition Test and the Raven's Coloured Progressive Matrices for the HIV positive group

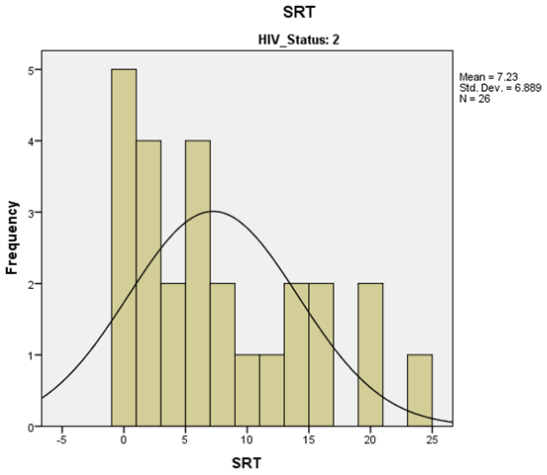


Figure 28. Histogram for Sentence Repetition Test for HIV positive group

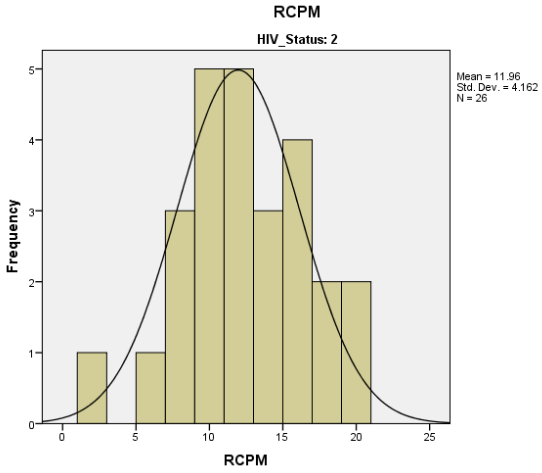


Figure 29. Histogram for Raven's Coloured Progressive Matrices for HIV positive group