THE EFFECTS OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ON THE COGNITIVE – LINGUISTIC ABILITIES OF ADULTS LIVING WITH HIV AND AIDS IN SOUTH AFRICA

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DECLARATION

I hereby declare that this thesis is my own, unaided except for the help given by persons listed under acknowledgements.

Signed this day in Johannesburg

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Anniah Mupawose

Date

DEDICATION

Firstly, I dedicate this thesis to my Lord and Saviour – Jesus Christ

This thesis is also dedicated to my parents Able and Naomi Rumano who have always encouraged and supported me to do "better", believe in myself and not settle in life. Dad I also want to thank you for sowing the seed in my life to do a PhD at a time in my life when I didn't even know what a PhD was - I just wanted to get through high school.

"...For I am what I am by the Grace of God" ***1 Corinthians 15:10***

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TABLE OF CONTENTS PAGE

LIST OF APPENDICES

PUBLICATIONS AND PRESENTATIONS IN SUPPORT OF THIS THESIS

Publication in Journal

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South African Speech and Hearing and Language Association, Annual General Meeting, May 2011

- Mupawose, A. The Cognitive – linguistic abilities of adults living with HIV and AIDS before and after highly active antiretroviral therapy (HAART).

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS USED

3TC	Lamiduvine
AIC	Akaiake information criteria),
AICC	Corrected Akaiake information criteria
ADL	Activities of Daily Living
ANOVA	Analysis of Variance
AR-1	Auto Regressive (1)
ART	Antiretroviral Therapy
ANI	Asymptomatic Neurocognitive Impairment
ASL	Arterial Spin Labelling
AVLT	World health Organisation (WHO)- University of California (UCLA) Auditory Verbal Learning Test
ARV	Antiretroviral
AZT	Zidovudine
BIC	Bayesian Information Criteria.
BBB	Blood brain Barrier
BOLD	Blood-Oxygen-Level–Dependant
BNT	Boston Naming Test
HO	Choline containing compounds
CLQT	Cognitive Linguistic Quick Test

CMV	Cytomegalovirus encephalitis
CTMT	Colour Trail Making Test
COWAT	Controlled Oral Word Association Test
CSF	Cerebral Spinal Fluid
CS	Compound Symmetry
CT	Computed Tomographic
d4t	Staduvine
DNA	Deoxyribonucleic Acid
EC	Endothelial Cells
EFV	Efavirenz
ELISA	Enzyme–Linked Immunosorbent Assay
fMRI	functional Magnetic Resonance Imaging
FWL	Four Word Learning test
GPB	Grooved Peg Board
HAART	Highly Active Antiretroviral Therapy
HAD	HIV Associated Dementia
HAND	HIV Associated Neurocognitive Disorders
^{1}HMRS	Proton magnetic resonance spectroscopy
ICF	International Classification of Functioning, Disability and Health

IHDS	International HIV Dementia Scale
IS	Interview Schedule
KPS	Karnosfky Performance Scale
MAP2	Microtubule-Associated Protein 2
MCMD	Mild/minor Motor Cognitive Motor Disorders
MRC	Medical Research Council of South Africa
MSM	Men who have Sex with other Men
NDOH	National Department of Health
NFL	Neurofilament protein
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
NNRTIs	Non-Nucleoside Reverse Transcriptase Inhibitors
OIs	Opportunistic infections
PCR	Polymerase Chain Reaction
PET	Positron emission tomography
PIs	Protease Inhibitors
PNS	Peripheral Nervous System
QOL	Quality of life
RHLB	Right Hemisphere Language Battery

RNA	Ribonucleic Acid
RPLT	Rotary Pursuit Learning Test
SEM	Standard Error Measurement
SMDT	Symbol Digit Modalities Test
STIs	Sexually Transmitted Infections
TMT A or B	Trail Making Test – Parts A and B
VF	Verbal Fluency
WAB	Western Aphasia Battery
WAIS	Wechsler Adult Intelligence Scale III
WAIS – BD	Weschler Adult Intelligence Scale Revised – Block Design
WAIS-DS	Wechsler Intelligent Scale – Digit symbols
WAIS - DSF	Wechsler Adult Intelligence Scale – Digit Span Test (forward)
WAIS - DSB	Wechsler Adult Intelligence Scale – Digit Span Test (backward)
WAIS-SS	Wechsler Intelligent Scales- Symbol Search
WHO	World Health Organisation
WMS	Wechsler Memory Scale – Revised
WVFRT	Word Verbal Free Recall Test

ABSTRACT

In the context of HIV high infection rate in South Africa, an assumption can be made that there is a high prevalence of HIV-associated neurocognitive disorders or cognitive linguistic deficits. The aim of this study was to determine assess whether highly active antiretroviral therapy (HAART) affected the cognitive – linguistic abilities of individuals living with HIV and AIDS before and after HAART use; and to determine whether their functional performance in terms of engaging in activities of daily living was affected by HAART use. Adults living with HIV and AIDs were recruited through purposive convenience sampling to participate in the study. They were divided into three groups. The experimental and cross sectional group included participants who were HIV infected and initiated HAART. The comparison group included participants who elected not to start HAART. Participants in all three group were assessed using the Cognitive – Linguistic Quick Test and were also required to fill out a structured interview scale at baseline, four and eight months. For the experimental group 55 participants were tested at baseline, 55 at four months and 52 at eight months after HAART initiation. The comparison group included 21 participants who tested at baseline, ten at four months and nine at eight months. The cross sectional group included different participants who recruited at baseline (55) before HAART initiation, then again at four (44) and eight months (42) after HAART initiation.

Descriptive analysis revealed that the mean scores for both the Cognitive – Linguistic Quick Test (CLQT) and the structured interview schedule (IS) in all the cognitive domains increased for all three groups from four and eight months after testing. However the severity ratings provided by the CLQT indicated that neurocognitive deficits were still prevalent among the participants after HAART intiation. The most impaired cogntive – linguistic ability was executive functions and the least impaired was language. One way ANOVA analysis on the CLQT and IS revealed that was a signiifcant difference in performance between the three groups at baseline, four and eight months. Repeated measures analysis revealed significant differences or improvements within participants across the three time periods. The greatest improvement was observed from baseline to eight months especially on the CLQT. ANCOVA analysis on the Cognitive- Linguistic Quick Test indicated that education had a major impact on cognitive – linguistic abilities followed by age and CD4 count. However, ANCOVA analysis on the structured interview scale revealed that the effect of time, participant group and to a lesser extent age influenced the participants cognitive – linguistic abilities when it came to perfroming activities of daily living. Quantitave inquiry using content analysis showed that participants in all three groups cited attention, followed by visual and language problems as hindering their abilities to perform activities of daily living.

The implications from this study revealed that even though HAART improves cognitive – linguistic abilities, neurocognitive deficits were still prevalent. Therefore findings suggest that health professionals need to monitor the neurocognitive impairments of their patients so as determine levels of functional performance.

Chapter 1: Introduction

Human immunodeficiency virus (HIV) infection results in an array of medical complications that particularly affect the central nervous system. It has been well documented that the HI virus is able to cross the blood brain barrier early on in the course of the disease progression and enter the central nervous system (Banks, 2005; Chiang et al., 2007; Eugenin et al., 2003; Fernandez, 2005; Hickey, Williams, Covey, & Woong-Ki, 2005; Kaul & Lipton, 2007; Miller, 2005). When HIV starts affecting the central nervous system it can result in HIV-associated neurocognitive disorders or cognitive-linguistic deficits. HIV-associated neurocognitive disorders can vary in severity from asymptomatic neurocognitive impairments to severe, debilitating HIV-associated dementia. These neurocognitive impairments can present themselves as difficulties in sustained attention, mental flexibility, information processing, memory, executive functions, language and psycho-motor speed (Cholewińska & Szymańska, 2009; Cloak, Chang & Ernst, 2004). HIV-associated neurocognitive disorders can also have a negative impact on the quality of life of an individual in that a person may not be able to perform their everyday activities of daily living or participate effectively in their social roles.

Despite enormous advances in the treatment of HIV-1 infection, the numbers of people who are HIV positive continue to rise. Since the first cases were first identified in 1981, almost 65 million people worldwide have been infected by HIV (Xia, Luo, Yu, Jiang & Liu, 2011). Among the 60 million HIV-infected individuals about 25 million of them have already died from the disease (Merson, 2006). It is also estimated that about 2.5 million become newly infected with HIV and 2.1 million people die of AIDS-related diseases every year (Xia et al., 2011). Furthermore, three-quarters of all people living with AIDS live in sub-Saharan Africa with South Africa having the highest number of HIV infections worldwide

(UNAIDS, 2008). HIV and AIDS is now considered a pandemic because it can be found on all the continents of the world.

HIV destroys the immune cell system of its host and eventually leads to acquired immunodeficiency syndrome (AIDS). There is currently no cure for HIV and AIDS, but there is treatment for HIV and AIDS in the form of highly active antiretroviral therapy (HAART). Notwithstanding the advances brought about by HAART, chronic infection of HIV-1 in the central nervous system (CNS) still occurs because not all antiretroviral drugs are able to permeate the blood brain barrier (Cholewińska & Szymańska, 2009; McArthur, 2004; Xia et al., 2011); hence the increased prevalence of HIV-associated neurocognitive disorders (HAND). Once the HIV virus enters the brain, it mainly invades the immune-fighting cells, microglia and macrophages in the CNS. These infected cells release neurotoxic substances that cause inflammation of brain tissue and nerve damage which leads to HIV-associated neurocognitive disorders (Cholewińska & Szymańska, 2009; Ernst et al., 2003), and in some cases progresses to HIV-associated dementia (HAD). HAD occurs in approximately 10-15% of all individuals with HIV and AIDS and is more common in the later stages of the disease (McArthur, 2004). The less severe disorders of asymptomatic neurocognitive impairments (ANI) and minor cognitive motor disorders (MCMD) are more common occurring in 30-60% of people infected with HIV depending on disease progression (Goodkin et al., 2001; Kaul& Lipton, 2007). HIV-associated neurocognitive disorders present themselves as difficulties in sustained attention, mental flexibility, information processing, memory, executive functions and psycho-motor speed (Cholewińska & Szymańska, 2009; Cloak et al., 2004).

Two strains or types of the virus have been detected namely, HIV-1 and HIV-2. HIV-1 is the more virulent and pathogenic (Williamson & Martin, 2010). HIV-1 mutates very rapidly and has a shorter latency period. This virus is commonly found in North and South

America, Europe, Central, East and Southern Africa (Whiteside &Sunter, 2000; Van Dyk, 2008). HIV-2 is associated with infections mainly in West Africa (Whiteside &Sunter, 2000; Van Dyk, 2008). HIV can be further classified into three groups - M, N and O. The M group is currently dominating the global epidemic because it is clustered in parts of the world that have the highest HIV and AIDS prevalence rates (Williamson & Martin, 2010). The M group of HIVs can be further sub-divided into sub-types or clades. Group M HIVs can be further subdivided into sub types or clades. There are currently nine clades named, A.B.C.D.E.F, G, H, J and K (Paul et al., 2005; Williamson and Martin, 2010). There are different subtypes in sub-Saharan Africa, with sub-types A and D predominant in Uganda and sub-type C predominant in South Africa and Europe. In contrast, sub-type B predominates in North America and in some countries in Europe (Sacktor, Nakasujja, Skolasky, Robertson, Wong et al., 2006).

Since the advent of antiretroviral therapy (ART), the effects of HAND or cognitive-linguistic deficits have improved significantly leading to decreases in the prevalence of HIV-related cognitive impairment (McCabe, Shread & Code, 2008). However, although ART has reduced the overall incidence of HIV-associated dementia, HAND continues to be a major clinical problem (Goodkin et al., 2001; Valcour& Paul, 2006). Although most HAND research has been conducted in the more developed countries of the West, the virus itself is most prevalent and least controlled in resource-limited countries in sub-Saharan Africa, and East and South Asia.

Findings from studies conducted in Western countries derive mainly from research on HIV-1 clade B infection found in the Caucasian populations, and therefore might not be generalizable to other HIV clades and to other ethnic peoples. A few studies have reported on HAND in Uganda (Sacktor, Nakasujja, Skolasky et al., 2009; Sacktor, Wong, Nakasujja et

al., 2005), but there are no studies that have investigated how specific cognitive-linguistic domains are affected by HAART and how these cognitive-linguistic abilities impact upon activities of daily living in the South African HIV-infected population. South Africa has the highest prevalence of HIV infections worldwide and is a region where HIV-1, Group M, clade C is predominant (Paul et al., 2005; Singh et al., 2010). Based on this information it can thus be assumed that HIV-associated neurocognitive disorders will also have a high prevalence rate in South Africa.

This research was conducted at an HIV and AIDS outpatient treatment clinic affiliated with a government health hospital situated in the province of Gauteng, the most populated and wealthiest province of South Africa. The participants recruited for this study were predominantly female, black, in their late thirties and early forties, unemployed with some secondary education irrespective of gender. All the participants were treatment naive at baseline that is they had not received any antiretroviral therapy at all. Participants were recruited into three groups. These three groups comprised an experimental, comparison and cross-sectional. There was a high attrition rate from baseline (110 participants) to 55 at four months and 53 at eight months for the experimental group. The baseline data for the cross-sectional group was collected from the 55 participants who did not return from the experimental group and had not initiated HAART. A different set of individuals was recruited at each time of testing at four and eight months after HAART use. The experimental and comparison groups were tested and followed up at baseline, four and eight months after HAART initiation. The comparison group included individuals living with HIV and AIDS not taking HAART. However, this was very difficult to do since some individuals elected to start HAART, or did not meet the CD4 count requirements to initiate HAART. The use of a cross-sectional group allowed some comparisons to be made when addressing the research aims.

Even though HAND have been identified in a similar HIV-infected South African cohort in another province using a cross-sectional design (Singh et al., 2010), to date no longitudinal studies investigating the effects of ARVs on cognitive-linguistic abilities have been conducted in South Africa. This research thus seeks to add to the body of knowledge with particular reference to South Africa about the assessment and treatment of HIV-related neurocognitive impairments.

These HIV-associated neurocognitive disorders are purported to be consistent with disruptions along the fronto-striatal (cortical-subcortical) circuitry (Paul et al., 2005; Woods et al., 2004). By means of various neuroimaging techniques, Ances et al. (2006), Berger et al. (2000), Ellis, Langford, and Masliah, (2007), Thompson, Dutton, Hayashi, Lu et al. (2006) and Thompson, Dutton, Hayashi, Toga et al. (2005) have documented that the HI virus can cause extensive damage to both the white and grey matter of the brain. HIV-associated neurocognitive disorders are usually identified through a number of different methods that include neuroimaging, cerebrospinal fluid examination, metabolic and/or toxicology screenings and formal neuropsychological testing. Of these methods neuropsychological testing has proven to be the most efficient and cost-effective method of identifying the different severities of HAND. The presence of HAND can have adverse effects on a person's quality of life in relation to their ability to perform functional everyday activities.

Many clinicians only assess the severity of HAND and fail to take into account how these neurocognitive impairments might influence an individual's ability to perform activities of daily living and participate in their immediate environment. This type of professional practice is under pinned by the International Classification of Functioning, Disability and Health Framework (ICF) of disability. HIV and AIDS can be considered a disability in that it

is a chronic condition - a person cannot be cured but treated. This framework was born out of the Biopsychosocial model or approach. Biopsychosocial model states that it is important to view an individual as a whole. That is in terms of how a human being interacts with his environment. The biopsychosocial model prescribes a systematic approach to understanding and treating the biological, psychological and social factors inherent in any human disease state (Cornwall, 2012). Therefore the guiding premise of this research states that it is not sufficient just to assess and treat, but to consider psychological and social factors that may have or are contributing to the individual's impairment or disability. In this case the assessment of HIV-associated neurocognitive disorders and how they affect a person's ability to perform activities of daily living.

1.2 Significance of the study

HIV and AIDS as a disease is here to stay unless a cure can be found to destroy the disease. It is well known that HIV and AIDS wreaks havoc in the body in many ways. The virus is able to cross the blood brain barrier and cause HIV-associated neurocognitive or cognitive-linguistic deficits. These HIV-associated neurocognitive disorders can range in severity from mild to HIV-associated dementia which is the most severe form. HIV-associated cognitive linguistic deficits are hypothesized to be mediated by cortical-subcortical neuronal loops, which originate in the cortex, extend in the basal ganglia through the thalamus and terminate in the cortex. It is therefore imperative that HIV-associated neurocognitive or cognitive-linguistic deficits are monitored for various reasons such as adherence to medication; and if not detected early could lead to HIV AIDS dementia a debilitating condition that requires substantial health services, that a country such as South Africa cannot extend due to the other burden of diseases already created by HIV and AIDS.

HIV-associated neurocognitive or cognitive-linguistic deficits can be assessed using imaging techniques such as functional magnetic resonance imaging (fMRI) or neuropsychological tests. Neuropsychological assessments are able to reveal the cognitive-linguistic skills (attention, memory, language, executive function and visual spatial skills) that might be impaired and are much cheaper to administer. This study set out to demonstrate that a neuropsychological test such as the Cognitive Linguistic Quick Test could be used to identify HIV-associated neurocognitive deficits. In the context of South Africa, which is a developing country, the most cost-effective, time-efficient and reliable methods of assessment are warranted to provide appropriate services.

By employing a longitudinal research design the researcher was also able to show that cognitive – linguistic abilities of individuals with HIV and AIDS do change over time i.e. become less identifiable when HAART is initiated. However, despite this change cognitive-linguistic impairments are still persistent. Furthermore, through survey enquiry, patients reported that that they were able to conduct their everyday activities irrespective of cognitive-linguistic difficulties. This is very consistent with cortical – subcortical lesions which present with abilities within functional limits, but impairments become more apparent with higher order cognitive tasks. These findings would not have become apparent if the researcher had only focused on the clinical abilities of the client. That is the structure and function of the individual as specified by the ICF. The ICF purports that it is important to determine how the impairments also affect an individual's ability to perform activities and participate in their environment. The individuals in this study were able to perform activities of daily living despite, the assessment indicating impairments. This alerts clinicians to not only focus on the results of an assessment because it does not provide information about an individual's

performance in their environment. This all forms part of the Biopsychosocial model. Knowing an individual's abilities both clinically and environmentally changes the management of an individual in terms of finances and time spent receiving services. Management becomes very client specific.

1.3 Assumptions

This study assumed that this South African cohort of individuals in attendance at this outpatient clinic was representative of those individuals with HIV and AIDS receiving health services from a public government facility. Patients would be available to be retested especially since they were being retested on days they were due to come for their medical check-up and refill of prescriptions. It was also assumed that the patients in both the experimental and cross sectional groups would improve their cognitive and linguistic abilities after HAART initiation.

1.4 Limitations and delimitations

It was very difficult to recruit participants for the control group. Obtaining a true control group was problematic, because as the CD4 counts drop immune system less able to fight off infection. So when an individual gets sick will opt to initiate HAART midway through the study. Attrition rate from baseline to four months was very high. Nurses at the clinic reported that patients in attendance at the outpatient clinic were very transient. Patients also did not always provide accurate contact information.

This research sort to determine the presence of HAND in individuals living with HIV and AIDS, with a CD4 count of approximately 250 cells/mm^3 and below, in attendance at a Government outpatient clinic. The aim of this investigation was not to determine when HAND becomes noticeable in an individual diagnosed as HIV positive irrespective of CD count or where they seek treatment.

1.5 Purpose of the study

The purpose of this study was to explore the effectiveness of HAART on adults living with HIV and AIDS through a longitudinal and cross-sectional method. So individuals had to be ready to initiate HAART. In addition the study also investigated the study whether HAART was able to provide any functional benefits in terms of activities of daily living in a South African cohort. To address this overarching aim the researcher assessed the cognitive – linguistic abilities of adults with HIV and AIDS before and after HAART initiation. It was hypothesised that HAART would positively affect the cognitive – linguistic abilities of adults living with HIV and AIDS due to its ability to decrease the viral load in the body.

The aims of the study were as follows:

1. To determine whether there is a significant difference in cognitive-linguistic abilities between the experimental, comparison and cross-sectional groups on the Cognitive-Lingusitic Quick Test and the interview schedule.

2. To determine whether there will be a significant difference in cognitive-linguistic abilities within the participants (time effect) for the experimental and comparison groups on the Cognitive-Lingusitic Quick Test and the interview schedule.

3. To determine the effect of variables on cognitive-linguistic functioning in both the experimental and comparison groups at baseline, four months and eight months on the Cognitive-Linguistic Quick Test and the interview schedule.

4. To describe the cognitive-linguistic abilities that affect performance and activities of daily living in the experimental, cross-sectional and control groups.

Chapter 2: Literature Review

2.1 Introduction

This chapter starts by providing a contextual background for this study. The background begins broadly by briefly examining the epidemiology of HIV in the world, and then takes a detailed look at the epidemiology of HIV in Africa, specifically in sub-Saharan Africa with particular reference to South Africa. A conceptual model which broadly frames this study will be provided. An overview of the HI virus will be presented including how it is managed and the ways in which it can result in HIV-associated neurocognitive disorders or cognitive-linguistic disorders. A definition of neurocognitive disorders will be given, followed by how these disorders are mediated and what the relationship is between cognition and language. Methods of assessment will then be discussed with particular emphasis on the measures used in this study and treatment of HAND. The conclusion of this chapter will culminate in a rationale and research questions pertaining to the study.

2.2 Background of HIV

This section provides a context and background of the study. It starts broadly, with global trends regarding HIV and AIDS, and then proceeds to Africa and sub-Saharan Africa, ultimately focussing on South Africa where this research was conducted. HIV and AIDS is discussed in the context of the burden of the disease, and other issues that exacerbate the prevalence of HIV and AIDS, particularly in sub-Saharan Africa and more specifically South Africa which has the highest number of HIV-infected individuals (Avert, 2010).

The world is now more than 20 years into the HIV and AIDS crisis with no cure in sight. Since the first reported cases of HIV and AIDS in 1981, more than 65 million people have been infected with HIV, and more than 25 million have died of AIDS (Merson, 2006). While numerous programmes have been set up throughout the world since the first cases were reported, the epidemic is nevertheless out of control. In addition this epidemic is mainly concentrated in the developing countries of the world such as Latin America, Africa and Asia where 95% of the 65 million people in the world living with HIV are located (Singhal & Rogers, 2003). Moreover many of the 25 million people who have died from AIDS lived in developing countries. On the contrary HIV infection rates and AIDS deaths have declined in richer and more developed countries; however infection rates continue to soar in developing countries (Singhal & Rogers, 2003). AIDS affects more people than it infects given that it has an impact on impoverished families as they try to meet the costs of patient care and funerals. In addition, AIDS has left behind orphans who are not only victims of the epidemic, but are also faced with the reality of an uncertain future.

As indicated earlier the 95% of people infected with HIV living in these minimally - industrialized countries, have very limited financial resources, resulting in an inability to manage and deal with the challenges presented by the HIV and AIDS epidemic. Furthermore these countries' hard-won social and economic development is most vulnerable to the heavy burden that HIV and Aids places upon them (Merson, 2006). AIDS is mostly a disease of poor countries because of the imbalanced distribution of health resources (D'Aesky, 2004; Cunha, 2007; Singhal & Rogers, 2003). Most people living with HIV and AIDS are in the economically productive age group (15 – 49 years) (Cunha, 2007;) and are the very individuals who have the potential and ability to play the financial supporting role to the children and elderly relatives within the family, however, sadly most will receive minimal

care when they finally develop AIDS-related illnesses. From many aspects the global HIV and AIDS epidemic is an enormous tragedy for humankind.

2.2.1 Burden of disease.

Although our understanding of the factors affecting the spread of HIV has increased, it seems we still do not fully contemplate why different parts of the globe have experienced such dissimilar HIV epidemics. Data on HIV prevalence in different countries has been compiled by UNAIDS (2008). Although the numbers vary greatly in quantity due to the discrepancies that exist in data collection (Gilks, 2001), they do, however provide us with some idea of the magnitude of the problem. Most care is delivered in health centres and community clinics, yet very little disease surveillance has been carried out at this level. Without knowing how much HIV and AIDS disease is presenting where and at what stage of disease progression, it is impossible to adequately describe the burden of care that the communities carry.

In high prevalence countries the additional burden of disease for HIV and AIDS is very vast and as it increases it is having a significant impact on the overall healthcare services and delivery of the basic primary healthcare needs of the people living in these countries. This is because the existing, pre-AIDS diseases (such as malaria, sexually transmitted diseases and TB) have not diminished in any way as the epidemic of HIV and AIDS disease has taken off (Holmes, Losina, Walensky, Yazdanpanah & Freedberg, 2003). There is no denying that AIDS infection rates have increased all around the world but the increase has been disproportionately high in sub-Saharan Africa as presented in Table 2.1. HIV has now been recorded in every region of the world. Below are a few global trends:

Table 2.1: Adults and children newly infected with HIV by region, 2008

Global HIV Infections, 2008			
Region	Adults and children newly infected with HIV	Global share of new infections (Percentage)	Percent of adults infected with HIV
Sub-Saharan Africa	1.9 million	71	5.0
South and Southwest Asia	280 000	10.4	0.3
Eastern Europe and Central Asia	110 000	4.1	0.8
Latin America	170 000	6.3	0.5
East Asia	75 000	2.8	0.1
Middle East and North Africa	35 000	1.3	0.3
North America	55 000	2.0	0.6
Caribbean	20 000	0.7	1.1
Western and Central Europe	30 000	1.1	0.3
Oceania	3 900	0.5	0.4
World	**2.7 million**	**100***	**0.8**

Percentages do not add to 100 due to rounding.

Source: Global Health Council: http://www.globalhealth.org/hiv_aids/global_view/

Sub-Saharan Africa

Sub-Saharan Africa has been more heavily affected by HIV and AIDS than any other region in the world. An estimated 22.4 million people are living with HIV in the region which accounts for 67% of all people living with HIV worldwide (Avert, 2010). In 2008 around I.4 million died from AIDS in sub-Saharan Africa which accounted for 72% of AIDS-related deaths and 1.9 million people became newly infected with HIV (Avert, 2010). The nine Southern African countries bear a disproportionate share of the global AIDS burden, with each having an adult prevalence greater than 10% (African Medical and Research Foundation (AMREF), 2010). Since the beginning of the epidemic, more than 14 million children have lost one or both parents to AIDS (Klimas, O'Brien Koneru & Fletcher, 2008). HIV has truly become a weapon of mass destruction that has reversed many of the hard-won development gains of the past.

In the absence of massively expanded prevention, treatment and care efforts, it is expected that the AIDS death toll in sub-Saharan Africa will continue to rise. This means that the impact of the AIDS epidemic on these societies will be felt most strongly in the course of the next ten years and beyond. Like an octopus with many tentacles, AIDS has reached and touched many aspects of African society, including those of socioeconomics, demographics and governance.

AIDS has also changed the face of African demographics in terms of gender dynamics, i.e. more women than men are being infected and the life expectancy has decreased since the advent of HIV and AIDS (Avert, 2010). More women of child-bearing age are HIV-positive than men (AMREF, 2010).Women are more likely to contract HIV on first sexual contact than men because their role in sex is to act as the receptor in receiving sperm that is already infected (Danziger, 1994; Evian, 2006). Furthermore, many African societies tend to be patriarchal in nature, where the male figure dominates in most aspects of

life. As a result sexual relationships are dominated by men, which ultimately means that women cannot always practise safe sex even when they are aware of the risks (Morison, 2001), and the unfortunate implication is that more women are likely to die from AIDS. This leads to a number of questions. Will statistics in the next ten years indicate an excess of adult males? Will there be an increase in commercial sex? Will these men seek increasingly younger women and girls as long-term partners?

From the above noted points and posed questions one could assume that it is evident that not only are more women being infected, but that the social impact of the disease is much greater on women than on men. While both men and women face enormous suffering as a consequence of the epidemic, the current social, economic, legal and political disadvantages experienced by women also heighten their vulnerability to the risk of HIV and AIDS (Danziger, 1994; De Waal, 2003; Global Health Council, 2009). For example, HIV-positive women are more likely to suffer violence or abandonment once their serostatus becomes known because they are held responsible for contracting HIV (Danziger, 1994; Gilks, 2001**)**. Of course this is an absurd allegation since it ignores the fact that the sexual transmission of the HI virus depends upon the sexual behaviour of both partners. Rejection and stigma experienced by women are compounded by their economic powerlessness, and legal disadvantages may include the lack of legal protection of property rights (Danziger, 1994). Impoverishment quickly follows, and is made especially painful when the women must find means of supporting their children while coping with deteriorating health.

Abandonment and rejection by the family of the husband can also occur if the woman's husband dies of AIDS even though she might have been the primary caregiver of the husband during his sickness (Danziger, 1994). This too can lead to impoverishment, especially if the partner's income was the primary source of income for the family (de Waal,

2003; Lurie, 2010). The issues surrounding a woman's rejection by the husband are similar if not identical to her being rejected by her husband had he been alive (Danziger, 1994).

In addition, the epidemic has also had far-reaching effects on women in their role as the primary caregiver within households. As the patient's health deteriorates, the physical and emotional burden placed on the caregiver becomes increasingly demanding. While coping with these problems women must at the same time meet their responsibilities of ensuring adequate food for the family and nurturing the young children in the family (Danziger, 1994). The enormous burden of care that has been placed on women because of home-based care has led (in some cases) to the neglect of their own health and well-being. Even young girls have felt the brunt of HIV and AIDS. Young orphaned girls are usually the first to be withdrawn from schools to assist with home duties and the care of younger siblings when parents die from HIV and AIDS (Danziger, 1994). Moreover, young girls and women are being encouraged or coerced to engage in sexual activities as men are seeking younger partners in an attempt to 'reduce their risk of HIV infection' (Lurie, 2010). The plight of women suffering from the social impact of HIV and AIDS can only improve if strategies and or policies are put in place to reverse women's social, economic and legal disadvantages.

The mortality impact of AIDS has also been significant. The life expectancy in sub-Saharan Africa before AIDS was approximately 62 years and increasing (Holmes et al., 2003). However, since the HIV pandemic, the life expectancy has dropped drastically to approximately 40 years and below in some countries (Holmes et al., 2003). The vast majority of people living with HIV and AIDS in Africa are between 15 and 49 and are thus in the prime of their working lives (Avert, 2010). This has had a profound impact on the economies of sub-Saharan Africa. As a result there are not enough people with sufficient work experience to effectively manage and operate private and government sectors. Productivity at

work has also been hampered in that people are calling in sick, attending funerals or caring for the sick. Meanwhile, morale at work suffers due to absenteeism and declining institutional effectiveness (De Waal, 2003). Monies are being spent to recruit and train new personnel to take over from people who are seriously ill or who have died. In some instances posts are left unfilled. In essence, private and government sectors are diverting funds from already haemorrhaging sections of the economy (De Waal, 2003) to deal with the epidemic.

Both HIV prevalence rates and numbers of people dying from AIDS vary greatly between African countries. In Somalia and Senegal, for instance, the HIV prevalence rate is under 1% of the adult population, whereas in Namibia, South Africa, Zambia and Zimbabwe prevalence rates are around 15 - 20%. In three countries the national adult HIV prevalence rate now exceeds 20%. These countries are Botswana (23.9%) (Avert, 2010), Lesotho, whose epidemic seems to have stabilized with a prevalence of 23.2% and Swaziland with one of the highest prevalence rate in the world of 26.1% (AMREF, 2009). West Africa has been less affected by HIV and AIDS, but some countries are nevertheless experiencing rising HIV rates. In Cameroon the HIV prevalence rate is now estimated at 5.1% and in Gabon it stands at 5.9% (UNAIDS, 2008). In Nigeria, HIV prevalence is low (3.1%) compared to the rest of Africa. However, because of its large population (it is the most populous country in sub-Saharan Africa), this equates to around 2.6 million people living with HIV (UNAIDS, 2008). Adult prevalence in East Africa exceeds 5% in Uganda, Kenya and Tanzania (Avert, 2010). Aforementioned have been some prevalence rates on HIV infection in Africa and sub Saharan Africa, the discussion going forward will focus on the country in which this study was conducted.

South Africa

South Africa has long suffered from the AIDS epidemic, and for decades epidemiologists and public health educators in South Africa have worked to understand and respond to the crisis. South Africa has been reported to have the highest prevalence rates of HIV infection in the world (Global Health Council, 2009; Gouws & Karim, 2010). The first two cases of AIDS were identified in South Africa in 1982 (Whiteside & Sunter, 2000). In the mid-1980s the first peak of the AIDS epidemic was predominantly diagnosed among white homosexuals. While the number of homosexuals diagnosed as HIV-positive began to plateau in 1989, the number of cases in the general population began to increase – so much so that between the years of 1990 and 1994 the number of heterosexual individuals with AIDS exceeded those who were homosexual (Karim & Baxter, 2010). As in most of Africa, the epidemic started as an urban phenomenon in South Africa that quickly spread to the rural areas. Since then the heterosexual epidemic has overshadowed the homosexual epidemic (Whiteside & Sunter, 2000). Life expectancy in South Africa is currently approaching 30 years of age for women and 34 years of age for men (Holmes et al., 2003, Avert, 2010). The impact of HIV and AIDS thus continues to have a devastating effect on the people of South Africa.

To understand the shape of the epidemic it must be understood that certain groups of South Africans are at a higher risk for HIV than others (see Table 2.2). In South Africa where race and socio- economic status are closely linked, the epidemic is mainly (98%) concentrated among the black population which makes up 90% of the total population (Singhal & Rogers, 2003). This has made black people more vulnerable to the infection, with women being at a higher risk for infection than men. Black women are more susceptible due to a mix of biology and gender-based power structures, as highlighted earlier, that may, for example, render condom negotiation with a partner difficult or impossible (Global Health Council, 2009).Adding to these cultural dynamics are their desperate economic situations,

which have forced women to become sex workers in order to survive (Karim, Karim & Baxter, 2010).

Table 2.2 HIV Prevalence by Population Group in South Africa, 2008

Population Group	Prevalence (%)
Black	13.6
White	0.3
Coloured	1.7
Indian	0.3

Source: http://www.avert.org/safricastats.htm

There might be a direct link between AIDS and four decades of apartheid where a racial system of structural violence was aimed at keeping the white minority, particularly Afrikaners, in power (Williams & Gouws, 2001). As a result of apartheid the black majority was marginalized and poor. Apartheid prevented millions of black South Africans from building a safe and secure life, a life exclusively possible for white South Africans. This inequality was strongly felt in the Health sector, as evidenced in the fewer hospitals, clinics, doctors or drugs being made available for black residents whether they lived in the townships or rural areas (Cunha, 2007: Gilks, 2001).

This legacy of an inadequate health care system from the apartheid era has left its traces which can still be seen today. The current living environments for most poor South Africans are unhygienic and unhealthy, characterized by high exposure to ordinary, as well as opportunistic pathogens. These pathogens are quite capable of causing significant morbidity

in immunosuppressed individuals diagnosed with HIV, even in its early stages (Gilks, 2001). Poverty among black South Africans also influences the disease presentation and quality of care. With few resources available, health-seeking behaviour may be significantly compromised and may be delayed, resulting in late clinical presentation which inevitably increases mortality even in readily treatable diseases (Cunha, 2007).

Gender inequality has been discussed with reference to the general spread of the disease among women in sub-Saharan Africa. However, with particular reference to South Africa, the issue of migration tends to add an additional dynamic to the HIV and AIDS burden that women tend to shoulder (see Table 2.3). In many instances poor women are forced to migrate from their rural areas or small towns to urban areas in search of employment in order to be able to support their children (Cunha, 2007). However, the majority of these women find that to supplement their low wages they often have to rely on transactional sex (Fassin & Schneider, 2003), predisposing them to sexual violence and HIV and AIDS.

Table 2.3: Estimated HIV Prevalence among South Africans by Age and Gender, 2008

Age	Male prevalence	Female prevalence
2 – 14	3.0	2.0
15 -19	2.5	6.7
20 – 24	5.1	21.1
25 – 29	15.7	**32.7**
30 -34	**25.8**	29.1
35 -39	18.5	24.8
40 – 44	19.2	16.3
45 -49	6.4	14.1
50 – 54	10.4	10.2
55 – 59	6.2	7.7
60+	3.5	13.6
Total	7.9	13.6

Source: The South African National HIV Survey 2008, Human Sciences Research Council

In 2007 South Africa accounted for 17% of the global burden of the disease and it currently has the highest prevalence of HIV-infected people in the world (Gouws & Karim, 2010), in relation to its population size. The disease burden has resulted in 605 480 HIV-

related deaths in South Africa from 1997 to 2006 (Avert, 2010). The South African National HIV Survey which was conducted by the National Department of Health in 2008 revealed that children, youth and adults had estimated prevalence rates of 2.5%, 8.7% and 16.8% respectively (Avert, 2010). The highest prevalence rate reported for women was 32.7% (25-29 years) and 25.8% (30-34 years) for men (Avert, 2010). This could be due in part to the increased vulnerability of women around the age of puberty as well as to the age difference in sexual partners (Gouws & Karim, 2010, p. 70). Young women tend to have older male partners which may explain the prevalence difference in age between men and women.

In October 2008, Statistics South Africa published a report titled "Mortality and Cause of Death in South Africa, 2006". According to this report, the number of deaths for 2006 due to diseases or conditions attributed to HIV totalled 605, 480. The data showed that between the years 1997 – 2004 the death rate among men aged 30-39 years doubled, while that among women aged 25-34 quadrupled (Avert, 2010). In 2006, HIV was recorded as the cause of death in 14 783 cases. However, the Medical Research Council of South Africa (MRC) has cautioned against the misclassification of deaths due to HIV. The MRC believes that these figures are a massive underestimation because individuals do not only die from HIV alone but other underlying causes (Nattrass, 2008). MRC researchers claim that many doctors only cite the immediate cause of death such as tuberculosis or respiratory infection for various reasons that could include not knowing the HIV status of their patients, or they may seek to conceal HIV infection to spare relatives the burden of stigmatization (Nattrass, 2008). Whatever the reasons, more accurate recording of HIV-related causes of death needs to be in place. Even though data recording measures are wanting in South Africa it cannot be denied that individuals are dying from HIV or AIDS related deaths. In an effort to reduce these deaths it is important to consider risk factors that put individuals at risk of contracting HIV in South Africa.

The two key risk factors influencing the spread of HIV infection in South are the migrant labour system and the high burden of other sexually transmitted diseases. South Africa has been recorded to have the highest prevalence of sexually transmitted infections (STIs) in the world (Coetzee & Johnson, 2010). Both HIV and STIs share the same mode of transmission - unprotected sex. Individuals with STIs are more susceptible to HIV infection for several reasons. Once an individual contracts an STI, the genitals are inflamed resulting in an increased presence of macrophages and T lymphocytes (Coetzee & Johnson, 2010; Evian, 2006).Moreover, ulcer-causing STIs disrupt the epithelial lining or barrier of the genitalia. So an individual with an STI who is HIV-negative is more susceptible to contracting HIV than an individual who is negative without an STI (Coetzee & Johnson, 2010). It has also been documented that "an HIV-infected partner sheds more virus in the presence of STI, thereby increasing the probability of HIV transmission" (Coetzee & Johnson, 2010, p. 217). Other factors that have contributed to the high prevalence of HIV have also contributed to the high prevalence of STIs. These factors include apartheid, an entrenched migrant labour system, gender and socio-economic inequalities.

In the past, South Africa's political economy relied heavily upon the migrant labour system to maintain the status quo of apartheid. Even after the dismantling of apartheid, it is currently estimated that there are more than 2.5 million legal migrants and many more illegal migrants drawn to work in South Africa's mines, factories and farms from rural areas within South Africa and from neighbouring countries (Lurie, 2010). According to Lurie (2010), "while the link between migrant labour and high-risk sexual behaviour has not been fully explored in detail in South Africa, it is clear that migrants' frequent and lengthy absences from home have more than likely disrupted their familial and stable sexual relationships. It has also been argued that the migrant labour system created a system for commercial sex in mining towns." (p. 149).

The historical and current context of HIV and AIDS in South Africa is important to consider because it is from this environment that the participants from this research were selected. Rosen, Ketlhapine, Sanne and Bachman de Silva (2008) investigated the characteristics of an HIV-positive urban population in South Africa who were accessing care and treatment from public hospitals in Gauteng and rural hospitals in Mpumalanga. According to the research of Rosen et al. (2008), a total of 1069 adults living with HIV and AIDS pre- and post-HAART were recruited to participate. They found that more women were diagnosed HIV-positive than men, and the majority of individuals were black, males were older in age (average 37.4 years) and the women were younger (average 33.6 years). The majority were unemployed with some secondary education. More than half the participants from the rural site reported that they did not read at all. They also found a low rate of marriage in their sample although they tended to have one long-term partner. These findings correlate very closely with some of the HIV and AIDS statistics that are presented in this chapter.

The HIV and AIDS epidemic has wreaked havoc in the African continent, especially in sub-Saharan Africa. As mentioned above, South Africa has the highest rate of HIV infection in the world and certain risk factors such as apartheid, socioeconomic and gender inequalities and an entrenched migrant system have enabled the virulent spread of the epidemic among the population. Since South Africa has the highest prevalence rates of HIV infection it can be inferred that it must also have a high prevalence rate of HAND including HIV-associated dementia (HAD) even though there are no national statistics to support this assumption.

Thus far the disease has been described in terms of its epidemiology with particular reference to South Africa, the context in which the study takes place. Following is a conceptual model for this study.

2.3 Conceptual Model

2.3.1 Introduction

The conceptual model underpinning this study is the Biopsychosocial model or approach. The wording model or approach will be used interchangeably. The general premise of this model is that any disease state (whether biophysical or mental) should be viewed in the context of how an individual interacts with their environment. In the case of this study how the resultant cause of HIV infection produces HIV-associated neurocognitive disorders (HAND) and how HAND affects a person in the context of their environment.

2.3.2 The Biopsychosocial Model

The biopsychosocial approach was first explained by George Engel in 1977. This model is based on a system approach. The systems approach was developed by Weiss and von Bertalanffy early 1950's (Engel, 1980). The systems theory approach basically asserts that "nothing exists in isolation. Whether a cell or a person, every system is influenced by a configuration of systems of which each is a part, that is, by its environment." (Engel, 1980, p.538).The biopsychosocial model was developed as an alternative to the traditional dogmatic biomedical treatment approach. Dr Engel was opposed to the reductionist view of disease that excludes the mind and environment. The reductionist view point of disease is at the cellular

and molecular level of a condition (Engel, 1980); the biopsychosocial model expands on this and refers to the interaction between the biological, psychological and social factors in the experience of a disease (Covic, Adamson, Spencer, and Howe, 2003).

The biological component of the biopsychosocial model recognises the biophysical or biological and mental conditions of the disease (Engel, 1977, 1980; Covic et al., 2003). The psychological component considers the personal psychological factors that can influence function and the measures an individual takes for his or her behaviours (Engel, 1977, 1980; Covic et al., 2003). The social recognises the importance of the environmental context, pressures and constraints (Engel, 1977, 1980; Covic et al., 2003). In essence this approach considers the individual, their health problems or disability within his/her immediate and broader environment.

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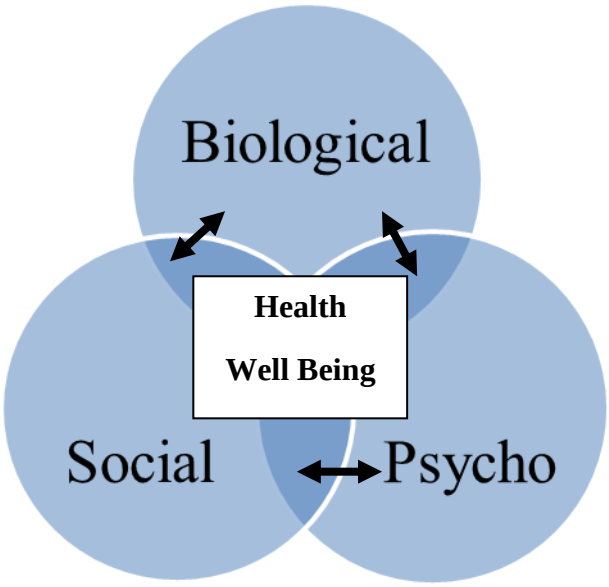


Source: Adapted from the CTC and Well Being centre. Retrieved from http//eitheory.com/2012/01/26/chronic-stress-and-biopsychosocial-intervention-stratgies/

Figure 2.1 Interaction of the three components of the biopsychosocial model

This is conceptually a comprehensive clinical model that can be applied to HIV-associated neurocognitive disorders especially in the context of this research as shall be shown with the proceeding sections of the literature review.

2.4 Adult Human Immunodeficiency Virus (HIV)

2.4.1. Introduction

This section describes the HI virus and how it progresses to AIDS. It further describes how the HI virus infects a human cell and replicates in the body. The section then continues with a discussion of the treatment of HIV and AIDS providing a historical overview of HIV and AIDS antiretroviral therapy with particular reference to South Africa. It is important to remember in this instance that ART initially started as monotherapy and progressed to triple therapy or highly active antiretroviral therapy (HAART). The section also shows how HIV, opportunistic infections and HAART can cause central nervous system damage that can lead to neurocognitive disorders and consequently, cognitive-linguistic disorders.

2.4.2 Human immunodeficiency virus.

A virus is a pathogen which is an organism that causes disease. Viruses cannot replicate and reproduce on their own because they do not possess the biochemical mechanisms to do so (Fan, Conner & Villareal, 2007) .Viruses are parasites and in order for them to replicate and multiply they need to live in tissue or cell types of a living body. Viruses are nothing but inactive lifeless and harmless chemicals (Fan et al., 2007). A virus consists of two main components: a core and a capsule or protective shell. Within the core

they carry genetic material which can either be DNA or RNA (Fan et al., 2007). The capsule acts as a vehicle that enables the virus to be transported from one cell to another. This is made possible by protein projections (or glycoprotein projections) or spikes that attach themselves to the host cell (Van Dyk, 2008). These projections attach themselves to specific receptor sites (or binding sites) of a host cell. Some viruses also have a third component, a lipid envelope that covers the virus (Van Dyk, 2008).

The HI virus is a retrovirus that has a circular shape. It is a retrovirus in that it encodes the enzyme reverse transcriptase (Fan et al., 2007). This unique enzyme is able to produce a DNA copy made from viral RNA, going against what is considered the normal flow of information, hence retro "to go back" (Morris & Cilliers, 2010). The virus is so small that 16 000 viruses can fit on a pin head. Its core RNA genetic material is covered by an envelope that has many small projections on its surface. These projections have an attraction to certain target cells with so-called CD4 receptor sites. These CD4 receptors are present on various types of blood cells including CD4 (helper) T lymphocytes, macrophages, monocytes, tissue cells (such as dendritic cells present in the genital tract and ano-rectal region), certain brain cells (glial cells) and other cells that have receptor cells (Kaul & Lipton, 2007).

HIV thus enters the body and destroys important cells which control and support the immune system. After entering the body, HIV attaches itself to the CD4 receptors, mainly dendritic cells and T lymphocytes (Fan et al., 2007). HIV can also attach itself to any of the abovementioned CD4 cells (Step 1). After binding to the CD4 receptor, the HIV envelope fuses with that of the CD4 membrane (Step 2). Once fusion has occurred, the viral capsule breaks open releasing the viral genetic material into the host cell (e.g. a CD4 cell) (Step 3).

An enzyme called reverse transcriptase converts the RNA which is a single strand to a double stranded DNA (proviral DNA) so that more viruses can be reproduced (Step 4). The proviral DNA fuses with the host DNA in the nucleus of the host cell with the help of the viral enzyme integrase and makes numerous copies of viral RNA and proteins (Step 5). Another viral enzyme protease enables these new viral DNA and proteins to assemble into new HI viruses (Step 6). As the new particles exit the cell, they kill the host cell in the process (Step 7). Then they move into the blood stream or surrounding tissue to infect more cells and repeat the process (Evian, 2006; Fan et al., 2007; Van Dyk, 2008).

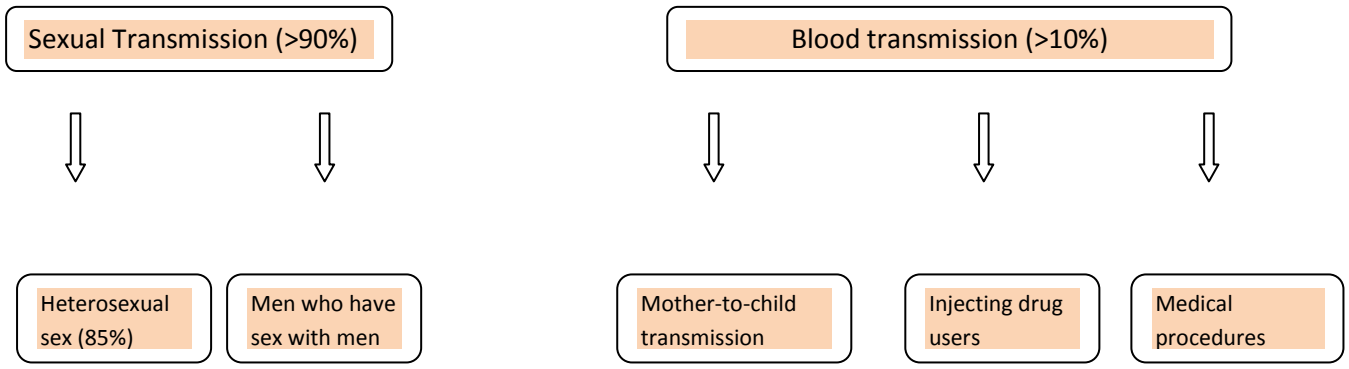
The body's immune system is a complex system of blood proteins and white blood cells that work together to protect the body from invading organisms such as bacteria, parasites, viruses, fungi and cancer to mention just a few pathogens (Fan et al., 2007; Van Dyk, 2008). The lymphatic system, the thymus gland and the bone marrow play an important role in the manufacture of blood proteins and white blood cells (Fan et al., 2007). The cells of the immune system can be divided into two main groups: Non-specific and specific defences (Fan et al., 2007; Van Dyk, 2008). Non-specific immune cells do not specialize in attacking specific pathogens but just provide a general defence to the body. If they fail to protect against the invading pathogens the specific defences are called in. The specific immune cells such as lymphocytes attack specific foreign pathogens or antigens. Antigens are proteins present on the surface of viruses or proteins. Lymphocytes, on the other hand, produce antibodies that attack specific antigens (Fan et al., 2007; Van Dyk, 2008). Antibodies are proteins produced in response to antigens to either destroy or deactivate them.

The immune system is a very well established and powerful system. It takes the HI virus a number of years to destroy enough of the immune system to cause immune deficiency and immune incompetence (Evian, 2006). According to Fan et al. (2007), HIV eventually is

able to overpower the body's immune system in several ways that include high mutation rates and latent states of HIV reservoirs. The HI virus has such a high mutation rate that the human body cannot produce antibodies that are able to neutralize subsequent viruses with mutated envelope proteins. Thus HIV is able to keep one step ahead of the immune system and continue to infect (Fan et al., 2007). In terms of latent states, the HIV is able to generate a reservoir of infected cells that are put on hold so to speak (made latent) to be activated at a later time by infectious microorganisms or infected HIV cells. These latent cells are able to circulate in the body undetected by human antibodies. Two modes of contracting HIV have been identified globally. These two modes of transmission are by sexual and blood transmission

2.4.3 Transmission of HIV.

. Sexual transmission accounts for how the majority (90%) of people contract HIV, (see Figure 1) (Global Health Council, 2009). Sexual transmission can either be through heterosexual sex or homosexual sex, that is, men who have sex with men (MSM). The other 10% of people with HIV contract the virus through blood transmission such as mother-to-child transmission, injecting drug users and medical procedures (Global Health Council, 2009). Since the scope of this study is on adults living with HIV, the following section on transmission will only discuss adult transmission.



Source: http://www.globalhealth.org/hiv_aids/global_view
Figure 2.2 Global modes of HIV transmission

Sexual transmission is by far the most common mode of transmission globally. During sexual contact, the virus can cross the mucosal barrier of the vagina, vulva, penis and rectum by first coming into contact with the immune cells that carry the virus across the mucosa (Evian, 2006; Klimas et al., 2008). The risk of infection during intercourse is greatly increased by concurrent sexually transmitted diseases, rough sex, or a partner with a very high viral load such as seen in primary infection and again in late stage disease. Women are generally more likely than men to acquire HIV during heterosexual intercourse due to the female physiological characteristics, such as the large amount of mucosal surface area the virus is exposed to which means it is two to three times more efficient in male-to-female transmission than female-to-male transmission (Evian, 2006; Morison, 2001). Receptive anal intercourse appears to be more risky than receptive vaginal intercourse with obvious implications for men who have sex with men (MSM) (Klimas et al., 2008). Therefore, the risks of HIV transmission are affected by frequency of sexual contact, condom use, immunological status, male circumcision and the presence of STIs (Klimas et al., 2008).

HIV is also spread by contact with infected blood, most often through the practice of reusing or sharing syringes and needles with drugs. This is also referred to as parenteral transmission (Morison, 2001). Effective community outreach and needle exchange programmes can reduce this risk. Parenteral transmission can also occur by the transfusion of infected blood; thus screening blood and/or reducing unnecessary use of transfusions are necessary to minimize transmission by this route (Morison, 2001). Occupational risk to healthcare workers also exists, mainly through accidental needle sticks or mucosal splash with contaminated blood (Klimas et al., 2008). The risk for occupational transmission varies depending on the type and severity of the exposure. The average risk of HIV transmission among healthcare personnel is estimated to be 0.3% after a needle stick and 0.09% after mucous membrane exposure (CDC, 2005).Once the HI virus is contracted via the different modes described, it starts to weaken the body's immune system progressively until it causes full-blown AIDS. The phases of the progression of this disease are discussed below.

2.4.4 Phases of HIV and clinical presentation.

There is a very special relationship between the viral load and CD4 cell count. The viral load refers to the level of HI virus in the blood stream. CD4 cells and viral load have an inverse "see-saw" relationship (Evian, 2006; Van Dyk, 2008). This means that the higher the viral load, the lower the CD4 cells because the virus destroys CD4 cells. A lower viral load will indicate a higher CD4 cell count, because if there are fewer viruses in the body, the immune system has a chance to build up CD4 cells.

The levels of HIV in the blood are highly predictive of the rate of disease progression; individuals with lower viral loads or set points progress more slowly than those with high

viral loads. It is not quite clear how the immune system of some individuals is not able to curtail viral replication or gain some measure of control over the virus and end up progressing to full-blown AIDS within two to three years of infection (Kopinsky, Stoff & Rausch, 2004). These individuals are said to be rapid progressors (Morris & Cilliers, 2010). The intermediate progressors are able to maintain good viral control for many years, but this cannot be sustained and the individual ultimately progresses to full-blown AIDS. This type of progression accounts for the majority of infections (Morris & Cilliers, 2010). Slow progressors are able to remain disease-free for an extended time period, for instance 20 years. They exhibit good viral control, i.e. very low to negligible viral load, which is due in part to a relatively intact immune system. Currently in South Africa there are very few slow progressors or long-term non-progressors (Morris & Cilliers, 2010).

Although HIV infection is theoretically divided into different stages, in practice these stages are not separate and distinct with easily identifiable boundaries. It is nevertheless helpful to divide HIV infection into the following stages as proposed by the World Health Organization (WHO) (2005): Pre-clinical stage - initial infection, clinical stage 1 - the asymptomatic stage, clinical stage 2 - the minor symptomatic stage, clinical stage 3 - the major symptomatic stage, and clinical stage 4 - AIDS-defining conditions.

The preclinical stage is called primary HIV infection, seroconversion illness or the acute phase. Initial infection is said to occur when seroconversion takes place. Seroconversion refers to the point at which a person's HIV status converts or changes from being HIV-negative to HIV-positive. This usually coincides with the time when an HIV test will show that a person is HIV-positive (World Health Organization (WHO), 2005). Seroconversion usually occurs six weeks after HIV infection. The HIV viral load is usually high in the first weeks after infection. Approximately 30% – 60% of individuals will develop

flu-like symptoms characterized by swollen glands, sore throat, headache, fatigue and joint pains which disappear after a couple of weeks (Fan et al., 2007; Van Dyk, 2008).

During the first stage of this disease an infected person displays no symptoms and the person is not even aware that they are carrying the HI virus. Even though the person displays no overt symptoms the virus remains active in the body and continues to damage and undermine the immune system. However, in some cases the only symptoms during this phase are swollen lymph glands (Evian, 2006; Fan et al., 2007). According to the WHO, a person in this stage can be placed on Performance scale 1, which indicates asymptomatic, normal activity, i.e. the person appears healthy and can carry on their work in a normal manner. This stage is associated with a CD4 cell count of between 500 – 800 cells/mm^3. The normal CD4 cell count in healthy, non-infected individuals is approximately 600 – 1 500 cells/mm^3 (WHO, 2005). Some individuals remain asymptomatic for long periods of time, respond well to medications, and undergo few infection-related complications until AIDS onset. A subset of these individuals, called long-term non-progressors are HIV-infected but they have a delayed progression toward disease as indicated by measures of CD4 cell loss, rises in viral load, onset to medical illness and may be to death (Kopinsky et al., 2004).

In the second stage the early clinical signs of HIV infection start to emerge. These include swelling of the lymph nodes in the neck, below the jaw, armpits and groin, shingles, skin rashes, fungal nail infections, recurrent oral ulcerations, recurrent upper respiratory tract infections, weight loss of up to 10% of the usual body mass, and lethargy (WHO, 2005). According to the WHO Performance scale 2, the person is able to carry on with normal activity despite being symptomatic. The CD4 count during this stage is between 350 – 500 cells/mm^3At Stage 3 the viral load becomes very high while the CD4 count becomes very low. Signs of more severe HIV-related diseases begin to appear caused by uncontrolled

multiplication of HIV itself (Van Dyk, 2008). Some symptoms include persistent and recurrent oral and vaginal candida or thrush, recurrence of herpes zoster or shingles, cold sores, fevers that last a month, night sweats, chronic diarrhoea, and significant weight loss - more than 10% of the body weight, reactivation of tuberculosis and opportunistic diseases of various kinds (WHO, 2005). According to the WHO Performance scale 3, the person will usually be bedridden for up to 50% of the day during the past month. The CD4 cell count is between 200 – 350 cells/$mm^{3.}$

By Stage 4 patients become infected by rare and unusual organisms that do not respond to antibodies. More persistent and untreatable opportunistic conditions and cancers begin to manifest themselves. HIV-related organ damage is also common at this stage of Acquired immune deficiency syndrome (AIDS) (WHO, 2005). When an individual has AIDS as a result of HIV, the body has a deficiency in the immune system – it cannot defend itself against disease or infection. AIDS is not a specific illness but a collection of many different conditions that manifest because the body cannot defend itself against disease-causing pathogens (Van Dyk, 2008). According to the WHO performance scale 4, patients will have been bedridden for more than 50% of the day in the past month. CD4 cell counts are below 200cells/mm^3. Hence the war against HIV and AIDS is futile unless some form of intervention is sought (Van Dyk, 2008).

2.4.5 HIV testing

The diagnosis of HIV is based primarily on the testing of blood samples. There are two types of blood sample tests; those that detect antibodies in the blood and those that detect the virus. The two most common HIV antibody tests are the enzyme-linked immunosorbent assay

(ELISA) and the Western Blot (Fernandez, 2005; Van Dyk, 2005). These tests cannot detect the virus but they do react to the antibodies that are formed in the body when the immune system tries to protect itself against the virus. The ELISA test is more widely used because it is cheaper, and yields very few false negatives (Van Dyk, 2008). In fact, a new generation of ELISA has now become available that simultaneously detects both antibodies and antigens (Van Dyk, 2008). Other forms of antigen testing fall under the umbrella of rapid HIV assay tests. These tests are more suitable for certain settings (such as rural, outreach situations or mobile clinics) because they are simple to perform, reliable and robust. In fact the results obtained from rapid tests are comparable to those conducted in a laboratory such as the Western Blot. Rapid HIV tests are not restricted to blood as in finger sticking, but can also use saliva or urine as specimens (Van Dyk, 2008). A major advantage of the rapid HIV tests is that results are available within 20 minutes (Puren, 2010). However, the results can only be used as screening measures and need to be followed up with more confirmatory tests such as ELISA. The two best known viral tests are the p-24 antigen and PCR (Fernandez, 2005, Puren, 2010). These tests yield results much faster than the antibody tests because they are not reliant on the body to produce antibodies.

In South Africa, a positive HIV diagnosis can be confirmed in various ways. It can be confirmed by two positive HIV ELISA tests based on separate specimens. Another method of diagnosis would include a positive ELISA test and a rapid HIV test. An alternative confirmation could include a positive ELISA test and a low CD4 cell count. The early diagnosis of HIV is important because in many cases the onset of AIDS can be drastically delayed if managed by antiviral drugs and living a healthier lifestyle (Minaar & Bodkin, 2006).

2.4.6 Management of HIV

Despite the gains in treatment, only one in five people in low- and middle-income earning countries who need antiretroviral drugs are receiving them (Merson, 2006). To restore the health of an HIV and AIDS-infected person it is necessary to suppress the replication process of HIV and rebuild the damaged immune system.

When HIV and AIDS was first diagnosed in 1981, antiretroviral drugs were not readily available. They only became available in 1987. The first antiretroviral medication approved for use against HIV and AIDS was AZT (zidovudine). In the mid- to late 1990s the use of triple drug therapy or highly active antiretroviral therapy (HAART) was introduced. The introduction of HAART has transformed the fatal infection into a chronic disease that is manageable in most patients (Egger, Boulle, Schechter & Miotti, 2005). Although the knowledge is available regarding the use of antiretroviral therapy, too many people especially in southern Africa do not have access to the drugs due to cost, lack of political will to roll out national treatment programmes and lack of trained personnel to effectively implement the treatment programmes (Egger et al., 2005; Zungu-Dirwayi, Shisana, Udjo, Mosala & Seager, 2004). Furthermore, due to the inaccessibility of antiretroviral therapy (ARV), the vast majority of HIV-infected people die around eight to ten years after infection, with tuberculosis being the most common AIDS-related illness (Morison, 2001).

Antiretroviral therapy (ART) is not a cure for HIV and AIDS, and it cannot prevent infection. The objectives of ART are to address virological, immunological, therapeutic and epidemiological problems that are caused by HIV and AIDS (National Department of Health (NDOH), 2010; Whiteside & Sunter, 2000). Virologically, ARV attempts to reduce the viral load as much as possible by interfering with the HIV life cycle (Van Dyk, 2008). Immunologically, ART serves to restore or preserve an individual's immunological function,

so as to reduce opportunistic infections. Therapeutically, antiretrovirals also aim to improve quality of life for an individual. Lastly, they serve an epidemiological function in that they reduce the impact of HIV transmission in the community. Effective ART has been shown to reduce the number of new cells infected by HIV and minimize its ability to develop drug resistance (Minaar & Bodkin, 2006).

Antiretroviral drugs are effective in reducing the presence of HIV-infected cells in the blood because they block the action of HIV enzymes. ART usually works in combination because of the nature of the replication cycle of the HI virus. When the virus enters the bloodstream it is harmless and needs to attach or fuse itself to a human white blood cell. The HI virus thus uses enzymes to fuse itself to the cell and replicate itself inside the cells (Mokgata, 2006). These enzymes include reverse transcriptase and protease (Minaar & Bodkin, 2006). Reverse transcriptase is responsible for the early stages of replication by transforming viral ribonucleic acid into viral DNA (Minaar & Bodkin, 2006). The viral protease enzyme plays the role of developing, replicating and maturing the virus.

There are currently five major classes of drugs currently available in the world which works to suppress viral replication. These include nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), entry inhibitors and integrase inhibitors (Lewthwaite & Wilkins, 2009). Entry and integrase inhibitors have been newly developed. Entry or fusion inhibitors block the fusion of the HI virus with the human cell plasma membrane so that the HIV core cannot enter the cell and infection is thus blocked at this step. Integrase inhibitors interfere with the enzyme responsible for HIV RNA replication into viral DNA, thus stopping viral replication (Lewthwaite & Wilkins, 2009). Entry and integrase inhibitors are not yet readily available in South Africa

(Van Dyk, 2008). Table 2.4 provides a summary of the classes of drugs currently available in South Africa, their effects as well as a list of the antiretroviral drugs.

Table 2.4: Classes of Antiviral Drugs and their Mechanisms of Actions

Classification of Antiretroviral Drugs				
	Nucleoside-reverse transcriptase inhibitor	**Non-nucleoside-reverse transcriptase inhibitor**	**Protease inhibitor**	**Fusion inhibitors**
Abbreviations	NRTIs	NNRTIs	PIs	FIs
Mechanism of action	Reverse transcriptase inhibition	Reverse transcriptase inhibition	Protease inhibition	Fusion inhibition
Specific action	Mimics the normal building blocks of HIV DNA	Directly inhibits reverse transcriptase	Inhibits late stage HIV replication	Binds to gp 41
Antiretroviral agents available in South Africa	zidovudine (AZT) (Retrovir) didanosine (ddl) (videx) zalcitabine(ddC) (Hivid) lamivudine (3TC) (Epivir) stavudine (d4T) (Zerit) abacavir (ABC) (Ziagen) tenofovir	nevirapine (NVP) (Viramune) efavirenz (EFV) (Stocorin or Sustiva)	indinavir (IDV) (Crixivan) saquinavir (Invirase) nelfinavir (Viracept) ritonavir (Norvir) amprenavir (Preclir) lopinavir/ritonvir (Kaletra) atazanavir	Enfuvirtide (T-20) Not available in South Africa

Source: *HIV and AIDS Care and Counselling,* (p. 98) A. Van Dyk, 2008, Cape Town: Pearson Education. Copyright 2008 by Maskew Miller Longman (Pty) Ltd. Reprinted with permission.

The National Department of Health (2010) has recommended that antiretrovirals be prescribed whenever possible where they provide maximum suppression of the virus so as to yield the best clinical results and prevent resistance. This can only be achieved by combining three antiretroviral agents resulting in highly active antiretroviral therapy (HAART). The National Department of Health has recommended two HAART regimes for the public health sector. Regime in this sense refers to a schedule or course of therapy or treatment. Basically the regime refers to the medication schedule or routine a patient will have to follow. Regime 1 (a) and 1 (b) consist of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTIs) as the first line of treatment. If Regime 1 fails, then patients are prescribed Regime 2 which consists of two NRTIs and one protease inhibitor (PI). If a patient fails to respond to both regimens, they are referred to an antiretroviral therapy specialist for individual evaluation and treatment. See Table 2.5 for specific drug regimes.

Table 2.5: National Department of Health Guidelines Treatment with Antiretrovirals

Regime	Drugs	Category	Indications
1 (a)	d4T plus 3TC and EFV	NRTI plus NRTI and NNRTI	For men as well as for women who are not of child-bearing potential or who are using injectable contraception plus condoms
1 (b)	d4T plus 3TC and NVP	NRTI plus NRTI and NNRTI	For women who are unable to guarantee reliable contraception whilst on ART
2	AZT plus ddl and lopinavir-ritonavir	NRTI plus NRTI and PI	For patients virologically failing Regime 1, despite demonstrated adherence

Source: *HIV and AIDS Care and Counselling* (p. 100), A. Van Dyk, 2008, Cape Town: Pearson Education. Copyright 2008 by Maskew Miller Longman (Pty) Ltd. Reprinted with permission.

It is important at this time to note several important facts about the success of HAART. These include side effects of the medications, interaction with other drugs and strict adherence. Like most drugs they can cause mild to severe long-term side effects depending on the tolerance level of the individual (Mokgata, 2006). These adverse effects are a serious concern to patients and health care providers. Concerns about metabolic complications, body shape changes and risk of cardiovascular disease are major threats to the success of HAART (Leen, 2003). Secondly, antiretrovirals have also been known to interact with other drugs as in the case of some TB drugs (Minaar & Bodkin, 2006; Van Dyk, 2008). Thirdly, dosing schedules and regimens are usually inconvenient and intrusive in a patient's lifestyle and may lead to poor adherence. Strict adherence and compliance to HAART is extremely important in achieving viral suppression and reducing the development of resistant strains. Fourthly,

delayed initiation of HAART because of the latter concerns poses certain challenges in that these patients present with a higher HIV viral load and a low CD4 count at HAART initiation and are thus likely to be more difficult to treat (Leen, 2003). Lastly, HAART at this time is unable to cure AIDS (Mokgata, 2006); it can, however, effectively keep viral loads to very low, almost negligible levels (NDOH, 2010; Fernandez, 2005). There is on going research to investigate the aforementioned facts and possible combination of HAART regimens to keep the viral load low. However, guidelines have been developed by the World Health Organisation (WHO) for global public health policy regarding the initiation of HAART (WHO, 2010).

2.4.7 Initiation of treatment.

HIV and AIDS is managed by following the progression of the disease. This is usually done by monitoring the virus in the blood by using PCR or p-24 testing. It is important to know the viral load in terms of knowing when to start antiretroviral therapy (ART), what type of drug therapy should be prescribed and assessing the effects of ART (Puren, 2010).

Initial guidelines recommended by the National Department of Health (NDOH) (2004) based upon WHO guidelines stated that HAART should be initiated if a patient or individual presents with symptomatic HIV-associated diseases such as unexplained weight loss, diarrhoea, and oral thrush to mention a few, regardless of CD4 count. HAART could also be initiated if the individual is asymptomatic with a CD4 count of 200cells/mm^3 or less. However, these guidelines also stipulated that treatment could be initiated when CD4 counts fell between 200-350 cell/mm^3 if the annual decline was more than the expected 20-80 cells/year, and in the case of rape. However, in 2009 the WHO revised their guidelines to

promote earlier intervention that includes initiating treatment at a CD4 count of 350cells/mm^3 for all individuals (All Africa, 2010).

The previous 2004 guidelines by the NDOH were also amended and revised in line with the 2009 WHO guidelines. The guidelines came into effect in April 2010, and due to the high cost associated with HAART, and the high burden of people in need of it in South Africa, treatment guidelines were extended to include earlier intervention for pregnant women, infants and those individuals that are co-infected with tuberculosis and HIV (NDOH, 2010).

The South African Joint Health and Treasury Task Team (SAJHTTT) (2003) reported that it the aim of the government had been to have a million people on ARV treatment by 2008 (SAJHTTT, 2003). Even though South Africa is considered as one of the most economically developed countries in Africa, this has not been reflected in the speedy roll-out of HIV treatment. In April 2004 the South African government embarked on an ambitious antiretroviral programme in response to the HIV pandemic, two years later than countries such as Botswana and Nigeria that had already started to issue HAART to the public in 2002. In 2006, 130 000 people were receiving ARV treatment in the public sector and 90 000 in the private sector, however approximately 79% of infected persons were still in need of ARVs in South Africa (Mokgata, 2006).

The South African National AIDS Council (SANAC), formed in 2006, had announced that its aim was to halve the HIV infections in the country and to provide treatment to at least 80% of the people and families living with HIV and AIDS (Van Dyk, 2008). However, apparently this initiative was not entirely supported by the reigning government or dispensation of the time. Since there is no accurate estimate of the number of people receiving treatment, it is difficult to determine the numbers still needing treatment currently. This is further complicated by the numbers of people who are initiated on ART but then drop out of

treatment. The best available estimates come from the Actuarial Society of South Africa model developed in 2003. By June 2008 it was estimated that 495 000 people were receiving ART with 520 000 still requiring treatment. In other words, the ART roll-out was then reaching less than 50% of the people who urgently required such treatment to stay alive (Aids Buzz, 2010). Fortunately it appears that this is changing with the 2010 figures, indicating a total of 791 000 adults and children receiving ART against the remaining estimated 702 000 that have not been initiated on ART or have dropped out of the programme (and so remain sick with AIDS).

Nonetheless, despite the efforts that have been made, there is still a long way to go if the high AIDS death toll (388 000 in 2010) is to be brought under control (Aids buzz, 2010). Efforts to provide ARV to people who need it have been hampered by a number of factors including shortage of competent staff, government's unbalanced budgetary priority structures resulting in the lack of government support for poorer provinces, and gaps in the dissemination of information between national and provincial departments, as well as civil societies (Ndlovu and Daswa, 2006). Examples of these gaps include lack of information pertaining to data collection and management, patient outcomes, patient numbers, and community awareness to mention just a few (Ndlovu and Daswa, 2006). Having said this, many South Africans and advocacy organisations have criticized the previous government led by President Mbeki and the late then Minister of Health Dr. Manto Tshabala-Msimang, as having contributed to the lack of proper processes that would ensure distribution and access of ARVs to the South African populous since they were considered to have presented mixed, delaying and denialist tactics, particularly in their approach to what they considered as solutions to addressing the prevalence and management of HIV and AIDS (Nattrass, 2008).

The South African National AIDS Council in 2008 proposed a national strategic plan which included its two main goals already articulated in 2006. This plan proposed, firstly, to decrease the incidence of HIV in South Africa by 50% and, secondly, to make sure that at least 80% of those eligible for ARV are accessing them (AIDS Foundation of South Africa, 2010). The best roll-out programmes for HIV and AIDS drugs have been in Gauteng, Western Cape and the North-West Province. KwaZulu-Natal and the Eastern Cape are increasing their roll-out numbers too. The rest of the provinces have been slow in making ART available to the public because of "poor management and political will" (Mokgata, 2006, p.2).

Nevertheless there now appears to be the commitment and political will of the current government under the leadership of President Zuma and the Minister of Health, Aaron Motswaledi, to correct the wrongs of the past (AIDS Foundation of South Africa, 2010). This positive level of commitment can only have positive outcomes for individuals living with HIV and AIDS in South Africa in terms of medical and neurological benefits. This also allows for research to be done regarding the effects of HAART on both medical and neurological conditions. It is imperative that research be conducted in developing countries such as South Africa regarding the effects of these antiviral drugs because most of the information gathered thus far comes from developed countries. Hence the value of conducting this research is to further add to the minimal knowledge and literature that has been generated regarding the effects of HAART on the cognitive-linguistic abilities of adults living with HIV and AIDS in South Africa.

2.4.7 The effects of HIV on the central nervous system

Although the HI virus has devastating effects on the body, this thesis is primarily concerned with how the virus affects the central nervous system to cause HIV-associated neurocognitive disorders that can result in cognitive-linguistic impairments. The HI virus impacts the CNS on three fronts - the disease, opportunistic cerebral infections due to bacteria, fungi and protozoa or viruses, and adverse effects caused by neurotoxicity of HAART (Ungvarski & Trzcianowski, 2000). However, one must bear in mind that HIV-associated neurocognitive disorders can be caused by the HI virus in the absence of opportunistic infections and HAART neurotoxicity.

There are two parts of the nervous system - the central nervous system (CNS) which includes the brain and spine, and the peripheral nervous system (PNS) which includes the nerves and muscles. The CNS has a natural protective barrier known as the blood brain barrier. The HI virus is able to cross the blood brain barrier (BBB) and enter the central nervous system within days of infection (Robertson et al., 2010). The BBB is composed mainly of specialized brain capillary endothelial cells (EC) in contact with astrocytes and is characterized by the presence of tight junction proteins between the EC and astrocytes. Low permeability is attributable in part to the presence of a highly developed tight junction between the endothelial cells and astrocytes in the absence of fenestrations (spaces) (Banks, 2005; Miller, 2005; Eugenin et al., 2006). These cells form a dynamic interface between the blood and brain.

CNS infection starts very early, in fact during the asymptomatic stage of infection. However, damage to the CNS seldom occurs until systemic immunosuppression is established (Kipnis, Derecki, Yang & Scrable, 2008; Xia et al., 2011). Infection can lead to brain swelling or inflammation, particularly of the brain lining or meninges. In medical terms

this is termed encephalopathy (Fan, Conner, &Villarreal, 2007). Monocytoid cells (macrophages, microglia, and monocytes) in the brain appear to be the prominent sites for replication. Brain inflammation can result for a couple of reasons. There can be an influx of immune system cells to fight the infection or a release from infected cells of the highly active toxic molecules called cytokines that can affect and kill brain cells (Alfano & Poli, 2002).

Despite extensive evidence of pathological changes in the CNS of infected individuals, the mechanism of viral entry into the brain is still not completely understood. However, there have been several theories posited as to how the virus crosses the BBB. These include the Trojan horse theory and the late invasion bone marrow theory. According to the Trojan horse theory, a few peripheral HIV-infected macrophages are able to pass through the BBB undetected, and once they cross they start to infect other cells, until a reservoir of latent HIV-infected macrophages are established (Berger et al., 2000; Portegies & Berger, 2007). These then become active and start to replicate and excrete neurotoxins, cytokines and proviral proteins. Later in the course of the disease these then cause HIV-associated dementia (HAD). Activation of this latent reservoir of infected cells can be caused by rising levels of HIV or viremia associated with opportunistic infections such as toxoplasmosis or cryptococcosis (Ungvarski & Trzcianowski, 2000).

On the other hand, there is now research to suggest that there is no reservoir of infected cells in the brain. This theory proposes that there is an initial wave of a few peripheral infected macrophages that cross the BBB and enter the CNS, particularly the brain, and as the disease progresses there is a later, larger, second wave of peripheral infected macrophages' that cross the BBB into the brain where they accumulate and eventually this leads to HAND (Fisher-Smith, Adeniyi, Rybicka, Morgello, Khalili, et al., 2004).

The bone marrow hypothesis suggests that HIV-infected cells make their way to the bone marrow where they are produced in mass. It has been suggested that this is a late-stage disease event (Goodkin et al., 2001). The bone marrow is one of the sites in the body where blood cells, predominantly white blood cells, are manufactured, so if infected white blood cells are transported via blood flow to the bone marrow, those will in turn end up infecting other white cells where they subsequently enter the circulatory system. Through the circulatory system the virus enters the brain and spinal cord (Hickey et al., 2005) and thereby contributes to HIV-associated neurocognitive disorders (HAND) (Goodkin et al., 2001). This, however, still remains to be documented either in Simian immunodeficiency virus monkeys or human patients.

Mechanisms of HIV-associated injury in the brain.

Regarding the mechanisms of HIV-associated injury, there is growing support to suggest that HIV-1 rarely directly infects neurons, but HIV or immune-related toxins cause indirect injury or death of neurons via a potentially complex web of interaction between macrophages (or microglia), astrocytes and neurons (Alfano & Poli, 2002; Giunta et al., 2006; Minagar, Shapshak, Fujimura, Ownby, Heyes & Eisdorfer, 2002; Nath, 2002)). Researchers claim that infected HIV white blood cells such as macrophages, monocytes and microglia's in close proximity of the blood brain barrier (BBB) release noxious substances such as nitric oxide, cytokines and arachnoid acid that cause the BBB to become permeable to the infected HIV cells; these infected cells once they have crossed the blood brain barrier then become reservoirs of HIV in the brain and the CNS (Minagar et al., 2002; Portegies & Berger, 2007). Once they cross the blood brain barrier, they excite astrocytes which are immune-fighting cells in the BBB to release neurotoxin substances along with infected HIV cells (Berger & Arendt, 2000; Eugenin et al., 2006**;** Giunta et al., 2006; Nath, 2002). These

infected cells produce proviral proteins such as Tat, HIV gp 41 and HIV gp120 along with cytokines that are released into the extracellular spaces of the brain. Extracellular space within the brain comprises 20% of the total volume of the brain volume (Nath, 2002).

Once the toxins have been released they interact with uninfected microglia's and macrophages to cause apoptosis (cell death or damage) (Hickey et al., 2005, Navia & Price, 2005). Neurotoxins also have an effect on neurons especially on the myelin sheath (Alfano and Poli, 2002; Karl and Lipton, 2005; Giunta et al., 2006). Larger neurons are more vulnerable to damage than smaller neurons (Wohlschaeger et al., 2009). Damage to the myelin affects the transmission of electrical impulses. Infected cells via proviral proteins are also able to cause uninfected monocytoids to release noxious substances such as intracellar Ca2+, cytokines and glutamate (Banks, 2005; Navia & Price, 2005). The neurotoxin effects of HIV can be seen by MRI using 3D mapping techniques.

There is no consensus in the literature as to whether the viral load (the amount of virus in the brain) and/or neuronal death corresponds to the development of HIV and AIDS dementia (HAD). Some researchers have suggested that there is an association between viral load and HAD as indicated by an association between reduction in volume of grey matter in the basal ganglia (Ances et al., 2006; Aylward et al., 1995; Thompson, Dutton, Hayashi, Lu, et al., 2006). Other researchers argue that the viral load or CD4 count does not determine the degree of HIV-associated neurocognitive disorders (Cook-Easterwood et al., 2007; Ellis et al., 2007; Price, 1998). Maybe the lack of agreement is due to the fact that most of these studies are conducted cross-sectionally, thereby making it difficult to come to a consensus about whether CD4 counts correlate with neuro-degeneration that can cause varying severities of HIV-associated neurocognitive disorders. The current study will shed more light

on whether CD4 counts correlate with cognitive impairments observed in HIV-positive patients considering that part of it has been conducted longitudinally.

However, this does not exclude the possibility that viral load at other time points during the course of the disease might be related to HIV-associated dementia (HAD). So if viral load is not consistently correlated to HAD this could suggest that secondary mechanisms may also play an important role in the manifestation of HAD. Wohlschaeger et al. (2009) propose that loss of neurons does not correspond to the absence or presence of HAD, but cognitive and motor deficits identified by neuropsychological tests seem to correlate well with neuronal damage (Thompson, Dutton, Hayashi, Lu, et al., 2006). In fact Ellis et al. (2007) suggest that synaptodendritic changes in HIV correlate closely with the presence and severity of cognitive impairment. Synaptodendritic injury is a specific type of neuronal injury that is not unique to HIV - it also occurs in diseases such as Parkinson's, Alzheimer's, schizophrenia, mood disorders and amyotrophic lateral sclerosis (Ellis et al., 2007). In HIV, although synaptodendritic injury is widespread throughout the brain, some regions of the forebrain show selective vulnerability.

Synaptodendritic injury comprises various structural and chemical changes that affect the ends of neurons – the synapses at which they communicate and interact with one another. Injury or insult to the dendrite can present as retraction of dendrite spines, dendritic beading (bulging or knotted appearance of dendrites) or aberrant outgrowths, all of which can occur without neuronal death (Ellis et al., 2007). The result of these pathological processes is a disruption or loss of normal synaptodendritic communication. Higher cognitive functions depend on a highly complex synaptodendritic network, and damage to this network results in abnormal output, measured as deficiencies in cognitive skills and behaviour. For example,

neurons that undergo dendritic beading lose their capacity for long-term potentiation, a central process in memory formation (Ellis et al., 2007).

Several techniques have been utilized to determine the degree of synaptodendritic injury. These include immunostaining, measuring synaptodendritic proteins or neuroimaging. The technique of immunostaining entails staining the proteins expressed in normal cell bodies and dendrites such as postsynaptic microtubule-associated protein 2 (MAP2) (Ellis et al., 2007). Results have revealed a reduction of MAP2 in the striatum (which comprises the putamen and caudate nucleus) and the hippocampus. This regional vulnerability parallels the higher burden of HIV proteins and viral RNA in the striatum and white matter connecting the striatum to the prefrontal cortex (Cook-Easterwood et al., 2007). Similar changes have been also confirmed by Cook-Easterwood et al. (2007) using SCID mice infected with the HI virus. They found that MAP2 expression was reduced in the brain areas immediately adjacent to infected macrophages.

Another technique or approach is to measure synaptodendritic proteins released from damaged neurons in the extracellular space which can be detected in the cerebral spinal fluid (CSF) or the blood. For example, elevated CSF neurofilament protein (NFL) concentrations are thought to indicate injury to myelinated axons. CSF NFL has been found to be high in persons diagnosed with HIV-associated dementia (Gisslen, Rosengran, Hagberg, Deeks & Price, 2005). However, it is not known whether increased levels of NFL truly reflect neuronal injury or whether NFL is dependent on cell death. There is no data as yet about the relationship between changes in neurocognition with HIV and changes in NFL.

Brain functioning can be impaired to varying degrees. Often the person will have difficulty concentrating, remembering, processing information or problem-solving. As the disease progresses, mental functioning can become more serious and reach a point where the

person becomes demented and is unable to take care of themselves. When this occurs the person is said to exhibit AIDS dementia complex or HIV-associated dementia (Grant, Sacktor & Mac Arthur, 2005).

To summarize the process of how the HI virus causes brain disease that results in varying degrees of neurocognitive impairment, Ernst, Chang and Arnold (2003) proposed a three-step process. The first step involves HIV infection that causes inflammation and brain injury, either directly due to the neurotoxic viral proteins (gp 120 and tat) or indirectly due to the deleterious effects of cytokines and chemokines (e.g. macrophage inflammatory proteins) that are released by HIV-infected microglia and macrophages and activated astrocytes (Kaul & Lipton, 2006; 2007). In the second step, brain inflammation and injury lead to metabolic abnormalities, some of which can be detected with modern neuroimaging techniques. For example, HIV-infected patients commonly show glial activation and proliferation which can be monitored with glial neuroimaging markers such as choline containing compounds (CHO), myo-inositol (MI) or proton magnetic resonance spectroscopy (H^1MRS) (Chang et al., 2004; Cholewińska & Szymańska, 2009; Ernst et al., 2003). In the third and final step of the model, cellular and metabolic abnormalities impair neural processing as evidenced by synaptodendritic injury and demyelization of the larger neurons (Chang et al., 2004; Ellis et al., 2007). To compensate for these impairments, affected individuals require increased attention (or neural processing) to maintain normal cognitive function, which can be detected and monitored by a blood-oxygenated level-dependant functional MRI, a direct and non-invasive technique to study brain function (Ernst et al., 2003).

Damage to the spinal cord can result in myelopathy or peripheral neuropathy. Myelopathy is the swelling of the spinal cord which can lead to weakness or paralysis of the limbs. Weakness or paralysis occurs because nerve impulses to the muscles from the spinal

cord have been disrupted (Fan et al., 2007). Peripheral nerve damage or neuropathy thus occurs when HIV-infected individuals experience swelling of the peripheral nerves (Fan et al., 2007). The specific causes of peripheral neuropathy in HIV are still unknown. Researchers suspect that either HIV or drugs that are toxic to the nervous system or a combination of both may be the cause of damage. The most common peripheral neuropathy is distal symmetric polyneuropathy (The Well Project, 2010). This happens when the communication between the nerves in the feet and/or hands to the brain and spinal cord becomes damaged. Individuals usually complain of numbness, burning or stinging sensation in the hands or feet (Fan et al., 2007; The Well Project, 2010). Cognitive dysfunction, peripheral neuropathy and myelopathy are not mutually exclusive. Individual patients may experience a mixture of any them. Moreover, it is not uncommon for HIV-1 to also precipitate cerebral vascular disorders such as infarcts, intracerebral or sub-arachnoid haemorrhage, strokes, subdural hematoma and transient ischemic attacks which can directly or indirectly lead to cognitive deficits.

Mechanisms of Opportunistic Infection- and HAART- injury to the central and peripheral nervous system.

Apart from the HI virus attacking the brain, opportunistic infections (OI), can also cause cerebral signs and symptoms that reflect cognitive deficits. Opportunistic infections are infections caused by agents or pathogens that would not have had any effect if the immune system was intact. These pathogens include bacteria, fungi, viruses, cancers and protozoa (Van Dyk, 2008). Those that can cause brain damage and alter mental state and sometimes cause generalized seizures include crytococcal meningitis (fungal), toxoplasma encephalitis (protozoa), cytomegalovirus (virus) and mycobacterium tuberculosis (bacteria) to mention just some examples (Alfano & Poli, 2002; Fan et al., 2007; Larson, 1998; McGuire, 2010).

Progressive multifocal leukoencephalopathy, primary CNS lymphoma and toxoplasmosis account for the majority of focal diseases that produce hemiparesis, hemisensory loss, visual field cuts, or disturbances in language use (McGuire, 2003). Some of the cognitive problems experienced by opportunistic infections include memory loss, poor concentration, decreased problem-solving abilities, slow processing abilities, personality and mood changes (Berger et al., 2000; Fernandez, 2005; Larson, 1998). A few of these disturbances have also been observed in patients on antiretroviral therapy (ART).

The brain tissue damage resulting in cognitive and language problems may be a side effect of antiretroviral therapy (ART), either directly because of central nervous system (CNS) toxicity or indirectly through side effects on other organ systems that impact the brain (Cardenas et al., 2009). The side effects of the medications prescribed in HAART can affect CNS and cause individuals to exhibit poor concentration, memory loss and sometimes hallucinations (Southern African HIV Clinicians Society, 2008). The drugs that might cause these problems include efavirenz (EFV) or stocrin. However, others such as zidovudine and staduvine can cause headaches, peripheral neuropathy and fatigue. Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al. (2009) found in their study of 102 HIV-positive individuals, that staduvine-based HAART caused peripheral neurotoxity, i.e. peripheral neuropathy. Protease inhibitors have been associated with cardiovascular disease, which in turn has been associated with the presence of lacunar infarcts and abnormal white matter in the brain (Cardenas et al., 2009).

To summarise this section, the HI virus enters the body insidiously and starts to replicate itself in immune cells that are supposed to be a defence mechanism against invading viruses or bacteria. Once an individual becomes HIV-infected, they do not automatically develop full-blown AIDS. There are a series of phases of symptomatology that an infected

person progresses through before developing AIDS. In developed countries where there are adequate health facilities and nutrition, the progression to AIDS is usually slower, ranging from 8-12 years, than in developing countries, where poverty, inadequate health services and poor nutrition are the prevailing norm and progression to full-blown AIDS is short - two to five years after diagnosis (Puren, 2010). Unfortunately access to HAART in South Africa for all individuals diagnosed with HIV and AIDS has not been fully realised. Once the HI virus is in the body its resultant effects are devastating. One of its effects on an individual is to cross the blood brain barrier and enter the brain and as a result cause HIV-associated neurocognitive disorders of varying severity. This research assumes that the presence of HIV-associated neurocognitive disorders can give rise to cognitive-linguistic deficits.

2.5 HIV-Associated Neurocognitive Disorders (HAND)

2.5.1 Introduction

This section defines neurocognitive disorders and how they are classified in HIV starting from the most subtle, asymptomatic neurocognitive impairments to the most devastating HIV-associated dementia (HAD). This section proceeds to describe in more detail the areas of the brain most affected by HI viral infection. The brain degeneration observed in HAND has also been observed in Parkinson's disease, Alzheimer's and normal aging (Cloak et al., 2004; Green et al., 2002; Marinus et al., 2003).Finally this section discusses the management or treatment of HIV-associated neurocognitive disorders. It is valuable to note that neurocognitive deficits seen in patients diagnosed with HIV can be caused by the HI virus, opportunistic deficits or HAART. The preceding sections described the three ways in which the disease can bring about HIV-associated neurocognitive disorders, which are

through the HI virus, opportunistic infections and neurotoxicity of antiretrovirals. The main focus of this section will be how the HI virus causes neurocognitive deficits that can give rise to cognitive-linguistic deficits.

2.5.2 Definitions.

Brain pathology that occurs due to HIV infection can produce behavioural impairments. These impaired behaviours are often indicative of CNS involvement and are termed neurocognitive processes and abilities (Dawes & Grant, 2007). Examples of neurocognitive processes include psychomotor speed and attention capabilities. Neurocognitive abilities are often grouped in terms of verbal language skills, executive functioning and abstraction ability, complex perceptual motor skills, memory, motor skills, and sensory functions (Dawes & Grant, 2007). When present, neurocognitive impairments can range in severity from subtle deficits to debilitating dementia. There are three diagnostic terms in common use to describe HIV-associated neurocognitive disorders (HAND). The first being Asymptomatic neurocognitive impairment, which refers to the presence of mild neurocognitive deficits that have been determined by neuropsychological testing and which have not progressed to the point where they interfere with everyday functioning – basically the individual is not aware of them (Ellis et al., 2007). The term "asymptomatic neurocognitive impairment" (ANI) is a more recent diagnosis in order to further differentiate subtle cognitive deficits from mild to moderate deficits. However, asymptomatic neurocognitive impairment is not a term that is widely used at present to denote neurocognitive deficits. Investigators tend to use the terms of mild/minor cognitive motor disorders (MCMD) or HIV-associated dementia (HAD) to describe HIV-associated neurocognitive deficits. Mild motor cognitive motor disorders indicate the presence of several

cognitive deficits that range from mild to moderate and which may or may not interfere with daily functioning (Fernandez, 2005). The majority of HIV individuals with mild motor cognitive motor disorders (MCMD) can typically continue to work and do other activities, albeit in a less than efficient manner. When the deficits are severe to profound it is termed HAD. These deficits render an individual incapable of living independently in the community.

According to Ciccarelli et al. (2011) and Thompson et al. (2005), at least 45% of HIV and AIDS patients suffer from neurocognitive impairments, ranging from asymptomatic neurocognitive impairment (ANI) to HIV-associated dementia (HAD), often with a progressive trajectory leading to death. HAD's progression to death is more rapid if the patient presents with advanced systemic disease, paralleling the immune defects and systemic effects of increasing HIV load and cytokine production (Grant et al., 2005). However, research has also revealed that individuals diagnosed with mild motor cognitive motor disorders (MCMD) are also at a high risk of mortality (Wilkie et al., 1998). It is interesting to note that not everyone diagnosed as HIV-positive develops dementia, and not everyone diagnosed with MCMD develops dementia (Thompson, Dutton, Hayashi, Lu et al., 2006). It is still not clear how an individual develops dementia, because high viral load has been detected in those areas of the brain that are the most affected, but neuro-degeneration has not occurred in those areas to produce cognitive impairments. Maybe this explains why not all HIV-positive individuals develop cognitive deficits or, if they do, they only present with asymptomatic neurocognitive impairment ANI or MCMD. The American Academy of Neurology (1991) cited in Fernandez (2005,) has developed clinical criteria for the clinical diagnosis of HIV-associated dementia (HAD) (see Table 2.6) and mild motor cognitive motor disorders (MCMD).

Table 2.6: Criteria for clinical diagnosis for HIV-associated dementia

Must have one of the following:
1. Acquired abnormality in at least two of the following cognitive abilities for at least one month: attention/concentration, speed of processing information, abstraction/reasoning, visual spatial skills, memory/learning and speech/language Cognitive dysfunction causing impairment of work or activities of daily living should not be attributable solely to severe systemic illness
2. At least one of the following: (a) Acquired abnormality in motor function or performance verified by clinical examination, neuropsychological testing, or both (b) Decline in motivation or emotional control or change in social behaviour
3. Absence or clouding of consciousness during a period long enough to establish the presence of item 1
4. No evidence of another etiology, including active CNS opportunistic infection or malignancy, other psychiatric disorders (e.g. depression), active alcohol or substance use, or acute or chronic substance withdrawal
5. HIV seropositivity (ELISA test confirmed by Western blot, polymerase chain reaction, or culture)

Source: From "The Ten Myths about HIV infection and AIDS" by F. Fernandez, 2005, *Focus: The Journal of Lifelong Learning in Psychiatry*, 3, 184-192. Reprinted with permission.

In patients with mild motor cognitive motor disorders (MCMD), cognitive impairments will manifest as changes in attention and memory registration, storage and retrieval as well as in psychomotor speed, information processing rate and fine motor function. However, these changes have minimal effects on activities of daily living and on functional performance status (see Table 2.7).

Table 2.7: Criteria for clinical diagnosis of HIV-1 associated minor cognitive motor disorder

1. Cognitive/motor/behavioural abnormalities (both of the following):

   (a) At least two of the following present for at least one month

   - Impaired attention or concentration
   - Mental slowing
   - Impaired memory
   - Slowed movements
   - In-coordination
   - Personality change, irritability, or emotional lability

   (b) Acquired cognitive/motor abnormality verified by clinical neurological examination or neuropsychological testing (e.g. fine motor speed, manual dexterity, perceptual motor skills, attention/concentration, speed of processing information, abstraction/reasoning, visual spatial skills, memory/learning and speech/language

2. Disturbance from item 1 causes mild impairment in work or activities of daily living

3. Does not meet criteria for HIV-1 associated dementia

4. No evidence of another etiology, including active CNS opportunistic infection or malignancy, severe systemic illness, active alcohol or substance use, acute or chronic substance withdrawal, adjustment disorder, or other psychiatric disorders

5. HIV seropositivity (ELISA test confirmed by Western blot, polymerase chain reaction, or culture)

Source: From "The Ten Myths about HIV infection and AIDS" by F. Fernandez, 2005, *Focus: The Journal of Lifelong Learning in Psychiatry*, 3, 184-192. Reprinted with permission.

2.5.3 HAND progression.

There is no consensus on the relationship between earlier (asymptomatic neurocognitive impairment and mild motor cognitive motor disorders) and later (HIV-associated dementia) neurological effects of HIV. Several models have been proposed in this regard:

- The milder neurological dysfunctions, cellular and molecular alterations seen earlier in HIV disease gradually accumulate, leading to full-blown dementia (Ellis et al., 2007). In other words, asymptomatic neurocognitive impairment (ANI) and mild motor cognitive motor disorders (MCMD) gradually progress to HIV-associated dementia (HAD) as in the case of Alzheimer's disease (Apostolova & Thompson, 2007). According to Chang et al. (2004), the pathological process begins with an inflammatory response caused by neurotoxic mechanisms localized in the white matter and basal ganglia, and progresses to neuronal injury and eventual neurocognitive impairment that leads to HAD.

- HAD only develops after some critical level of CNS damage is reached as in the case of Parkinson's disease. Parkinsonian symptoms develop only after 80% or more of the substantia nigra neurons are lost (Grant et al., 2005).

- Early mild motor cognitive motor disorders (MCMD) represent a relapsing remitting condition early on, with progression to HAD in only a subset of HIV-positive individuals later on. This is similar to the progression of multiple sclerosis (Fisher-Smith et al., 2004).

- MCMD represents a process separate from the more HIV dementia. This is similar to the alcohol brain disease model – many alcoholics' exhibit neurocognitive impairments. Wernicke-Korsakoff syndrome occurs in only a few later stage alcoholics and its pathogenesis involves mechanisms that are different from the common variety of neurocognitive impairments observed in other pathologies (Grant et al., 2005). More sophisticated research methodologies are needed that examine neuropsychological performance, markers of systemic immune function, and HIV

replication to fully understand how ANI, MCMD and HAD become evident in the body.

2.5.4 Incidence and Prevalence Rates

Prevalence and incidence rates of mild motor cognitive motor disorders (MCMD) and HIV-associated dementia (HAD) are readily available in developed countries such as the United States of America but not in African countries. This is due to the limited resources available in terms of manpower or skilled professionals and equipment to assess HIV-associated disorders; there are thus no accurate rates available for Africa, and therefore most of the data that is used is based on American data.

In terms of incidence and prevalence rates, more people are diagnosed with MCMD than HAD. Initially before the advent of HAART, the incidence and prevalence of HAD was considered to be very high. Initial reports on the prevalence of dementia in AIDS varied from 7% to 66% depending on the referral population studied and the selection criteria used. Since the introduction of HAART, all reports on the incidence of HIV-associated dementia (HAD) indicate that HAD has decreased but not to the level where the presence of HAD has been eliminated (Ances et al., 2006; Shiramizu, Williams, Shikuma and Valcour et al., 2009).

Other reports go as far as to say that the incidence and prevalence of HIV-associated neurocognitive disorders is on the rise, possibly due to drug resistance and limited CNS penetration of some antiretroviral drugs and poor drug adherence (Cysique, Maruff & Brew, 2004; Wohlschlaeger et al., 2009). Furthermore, research has shown that HAART is unable to stop the infiltration of infected macrophages into the brain, and it is not able to cross the blood brain barrier to prevent the replication of infected cells in the brain (Kaul & Lipton, 2006, 2007; Shiramizu et al., 2009). However, the benefits of HAART should not be

understated, and HAD has decreased by 50% since the introduction of HAART (Sacktor, Nakasujja, Skolasky, Robertson, Wong et al., 2006).

Estimates of the percentage of HIV-infected individuals diagnosed with HIV-associated dementia (HAD) vary greatly (Minagar et al., 2002; Wohlschlaeger et al., 2009). The data collected (pre-HAART) prospectively in the Multicentre AIDS Cohort Study revealed an incidence of 7% within 12 months of the diagnosis of AIDS and 14% within two years of AIDS onset (McArthur et al., 1993). The cumulative life time risk of developing HAD was 5-20% pre-HAART (Wohlschlaeger et al., 2009) and as many as 60% of HIV and AIDS patients may have some level of neurocognitive impairment by the time of death. Since the advent of HAART in 1996, the incidence of HIV-associated dementia (HAD) has decreased by 50% (20% -10%) while the prevalence rate has increased from 6.6 in 100 in 1994 compared to 10.1 in 100 (Cook-Easterwood et al., 2007).

The sustained prevalence of HIV-associated neurocognitive disorder might be due to drug resistance and poor adherence. Njamnshi et al. (2009) reported that the national prevalence of HIV-associated neurocognitive disorders including HAD was higher than 21%. They proposed that this prevalence could be the same or higher in sub-Saharan Africa. This may most likely be the case since initiation of HAART is rather late in terms of disease progression as compared to developed countries. In addition not everyone in sub-Saharan Africa has access to HAART so as to reduce the prevalence of HIV-associated neurocognitive disorders. This high prevalence of HIV-associated neurocognitive disorders could also be indicative of the prevalence of cognitive-linguistic impairments.

2.5.5 Clinical Presentations of HIV-Associated Neurocognitive Disorders and Neuropathogenesis

The clinical and neuropsychological abnormalities of HIV-associated neurocognitive disorders can reflect in all or one of three areas depending on the severity of the neurocognitive disorders. These three areas include cognition, motor and behaviour. Cognitive impairments are characterized by mental slowness, forgetfulness, poor concentration, difficulty processing and acquiring new information, difficulty with tasks requiring "executive functions" (i.e. complex cognitive tasks requiring planning, set shifting, and coping with novel situations) and poor sequential processing (Grant et al., 2005; Larson, 1998; Storace, Dijkgraaf, Houweling, Postma & Tramarin, 1998). Motor symptoms which are due to basal ganglia damage include a loss of fine motor control leading to clumsiness, gait disturbances (poor balance), impaired postural reflexes, and tremors. Behavioural changes may include apathy, lethargy, depression and diminished emotional responses and spontaneity (Berger & Arendt, 2000; Price, 1998). Berger and Arendt (2000) further add that it is not uncommon to see individuals with HIV and AIDS exhibit postural instability, rigidity, hypomimetic facies, hypophonia, dysarthria (poorly articulated speech). Even in the absence of apparent cognitive impairment, HIV-infected patients may demonstrate sub-clinical motor dysfunction indicative of basal ganglia dysfunction. Evidence of the latter includes slow reaction time, postural imbalance, and impairment of rapid alternating index finger movements and extensions (Berger & Arendt, 2000). In fact quite a few tests use psychomotor abilities as an early indicator of the presence of neurocognitive deficits in individuals living with HIV and AIDS.

The neuropathogenesis of clinical presentations are purportedly subserved by neuronal loops extending from the cortex to the subcortex (Woods et al., 2004). HIV-associated neurocognitive disorders reflect neurotoxic mechanisms that cause disruptions

within the circuits connecting the frontal lobes and basal ganglia (Woods et al., 2004). Due to advances in imaging techniques such as fMRI, PET, CT scans and physiological techniques such as cell recording and neuronal tracing, substantial evidence for promoting the involvement of subcortical structures not only in motor movement but also in cognitive and language processes is now emerging(Koziol & Budding, 2009). Researchers are thus now proposing a vertical or fronto-subcortical approach to studying HIV-associated neurocognitive disorders and cognitive linguistic deficits (Murdoch & Whelan, 2009).

Technological advances have also significantly improved our understanding of neuronal structures, their connective patterns and how structures relate to cognitive functioning. Neuronal connections between regions of the cortex and basal ganglia have been identified. These neuronal networks provide the anatomic substrate for supporting not only motor, but also cognitive and behavioural functions (Middleton & Strick, 2000). The neuronal "loops" or circuits originate in the cerebral cortex. After passing through the various subcortical structures within each respective system, the circuit re-enters the cortex and terminates very near the same region in which the circuit originated (Koziol & Budding, 2009). Therefore a general feature of this circuit is the fronto-basal ganglia/striatal loop of interaction.

Convergent evidence for the role of fronto-basal ganglia system's neuropathysiology in HIV-associated neurocognitive disorders is provided by neuroimaging studies in HIV. Regarding the basal ganglia, studies have revealed atrophy of the caudate nucleus (Thompson, Dutton, Hayashi, Lu et al., 2006) and substantia nigra (Berger et al., 2000), and enlargement of ventricular spaces. In addition, smaller caudate volume is associated with HIV disease (Alyward et al., 1995; Ances et al., 2006), and smaller caudate volume correlates with poorer performance on cognitive tests in patients with advanced HIV disease

(Thompson et al., 2006). Due to the subcortical involvement, HIV-associated dementia is considered to be a "sub cortical" dementia consistent with the dementia observed in Parkinson's disease and Huntington's chorea (Berger et al., 2000; Marinus et al., 2003; Thurnher et al., 2000). However, cortical regions are not spared, and investigators have clearly shown that in HIV and AIDS cortical damage occurs via neuronal loss and synaptodendritic simplification (Ellis et al., 2007).

Cortical degeneration has been found to be consistent in patients with HIV and AIDS in terms of volume loss in the medial frontal and pre-motor cortices; and thinning of the prefrontal and parietal cortices in particular has been associated with the severity of neurocognitive impairment in AIDS (Thompson, Dutton, Hayashi, Toga et al., 2005). Thompson, et al. (2005) and Chiang et al. (2007) have extended their investigations of HIV and AIDS patients to include degeneration in white matter regions of the brain underlying the primary association and sensorimotor cortices. Degeneration in these regions has been linked to a reduction in information processing speed and higher cognitive deficits in HIV-positive individuals. Furthermore, 3D imaging techniques have revealed white matter atrophy especially of the frontal areas of the corpus callosum, hippocampus and cortex starting early in the asymptomatic stage, and accelerating in atrophy towards the latter stages of HIV (Apostolova & Thompson, 2007; Thompson, Dutton, Hayashi, Toga et al., 2005; Thompson, Dutton, Hayashi, Lu et al., 2006; Wilkie et al., 1998; Wohlschlaeger et al., 2009). Finally functional magnetic resonance imaging (fMRI) studies have also found functional changes in the prefrontal cortical regions during tasks of attention and working memory (Thompson, Dutton, Hayashi, Toga et al., 2005). Together all these studies provide evidence that HIV is associated with changes in the cortical and subcortical regions.

Despite all the research that is being done, there is no consensus in the literature as to the progression of HIV-associated neurocognitive disorders (HAND). Aylward et al. (1995) and Cloak et al. (2004) report that atrophy starts with the cortex and progresses to the subcortex, particularly the basal ganglia, whereas Wilkie et al. (1998) and Grant et al. (2005) are in consensus and report that damage starts as a subcortical process which then evolves and becomes more pronounced in the cortical structures as the disease progresses. Perhaps a lot depends on the sensitivity of the instrumentation utilized to examine the brain's neurodegeneration. However, an assumption can be made that atrophy starts subcortically and progresses to the cortical regions due to the fact that patients can present with motor deficits without the presence of cognitive impairments. Conversely, Aylward et al. (1995) argue that HIV patients can exhibit white matter atrophy, with limited grey matter involvement, because HIV-positive patients who exhibit dementia present with more white and grey matter atrophy volume. Therefore more longitudinal studies need to be designed to determine where and when degeneration starts and progresses to in the brain.

2.6 Relationship between HIV-Associated Neurocognitive Disorders and Cognitive-linguistic Abilities

2.6.1 Introduction

In this section the relationship between cognition and language is discussed, how they are subserved by fronto-basal ganglia circuitry, and what evidence there is to support this in HIV and AIDS research infers that neurocognitive functioning is directly related to cognitive-linguistic functioning. To highlight this relationship, terms need to be defined and theories explored.

2.6.2. Definitions.

This research straddles the disciplines of neuropsychology and speech language pathology, and to some extent cognitive psychology. There are certain terms that are specific to neuropsychology such as neurocognitive processes and abilities; and certain terms that are specific to speech language pathology such as cognitive-linguistic abilities. The neuropsychological perspective defines neurocognitive processes and abilities as behaviours that are indicative of CNS involvement due to brain pathology caused by HIV and AIDS (Dawes & Grant, 2007). Whereas the speech language pathology perspective would view cognitive-linguistic problems in light of how brain pathology, in this case diffuse brain damage caused by HIV and AIDS, affects the interaction between language and cognition (Murdoch & Whelan, 2009).

At this point of the discussion it would be appropriate to start defining terms or concepts. Cognition is a general term that refers to both stored knowledge (memory) and the mental process of knowing, including aspects such as awareness, perception, reasoning, and judgment. In fact, cognition can be viewed as a company with many departments working together to process information (Bayles & Tomoeda, 2007). These departments, mental processes or domains usually include but are not limited to attention, executive functions, memory, visual spatial and language.

Regarding language, certain distinctions need to be made between terms, that is, – communication versus linguistic communication, language, and speech. Communication is the exchange of ideas or thoughts between individuals that can either be verbal or non-verbal as in gesturing or writing(Owens, 2004; Reed, 1986).It is considered linguistic when words are used and non-linguistic when other symbols are used, such as writing and gesturing (Bayles & Tomoeda, 2007). Therefore, language refers to the symbol system by which sound

is paired with meaning to form words for a particular purpose (Owens, 2001). Just as gesturing or writing relies upon movements in proper order, vocal speech sounds need to be organized in proper sequence to convey proper meaning (Bayles & Tomoeda, 2007). In this way, "speech" or oral language is very closely tied to motor sequencing systems.

Vocalizations rely upon serial-order processing or motor sequencing. This fact alone already provides some hint that sub-cortical brain regions most likely play a role in language. Whereas "linguistic communication" is the cognitive process of sharing ideas through language (Bayles & Tomoeda, 2007), there is evidence to suggest that cognition, language and speech production share neural mechanisms (Pickett, Kuniholm, Protopapas, Friedman & Lieberman, 1998). For example, the simple act of object-naming or recognition requires perception, access to long-term memory, association, recognition, lexical retrieval, decision-making, motor planning and self-monitoring (Bayles & Tomoeda, 2007). This example lends more support for the premise that cognition, language and speech are mediated by cortical and subcortical areas of the brain.

2.6.3 Theories on the relationship between language and cognition.

Few people would disagree that language and cognition are related. However, there is no universal agreement concerning the nature of the relationship. Several theories have been proposed to explain the relationship between language and cognition. There has been a body of work proposed by Piaget and others which postulated that cognition precedes the development of language and those certain cognitive precursors need to be in place before language can develop (Owens, 2001). In essence cognitive growth is responsible for language. Therefore any linguistic behaviour has to be undergirded by cognitive processes.

While cognition and language are interrelated, cognition is clearly the dominant member (Owens, 2001). A related view of language functioning as dependant on cognition is the weak cognition view. This position proposes that cognition accounts for much of an individual's language abilities but not all of them. There remain some aspects of language which do not derive directly from language such as language difficulties with expressing meaning (Reed, 1986).

Another point of view concerning language and cognition proposes that, although language and cognition are related, cognitive activity without language and language without underlying cognitive bases are both possible. According to Vygotsky (1962) as cited in Reed (1986), language and cognition are interconnected processes that develop and occur simultaneously. Vygotsky theorized that thought and language have different genetic origins and separate curves of development. At a certain age these two processes converge and start to develop simultaneously (Owens, 2001). Cognition and language are processes that are dependent on each other. Some researchers have observed that certain cognitive and linguistic skills develop at the same time, but not necessarily in a predetermined order. In other words, language sometimes emerges first, and in other instances cognition does. These observations have led to the position that language and cognition are distinct functions that derive from a common, but separate source – the homologue model (Reed, 1986). Therefore if cognition is impaired, language is inadvertently impaired too.

Another theory that has attempted to describe the relationship between language and cognition is linguistic determinism proposed by Benjamin Whorf. This position states that "all higher thinking is dependent on language, language determines thought" and that the more lexical richness or breadth in a language, the more superior the resultant cognitive development" (Owens, 2001, p. 132). However despite all the theories that have been

postulated describing the relationship between cognition and language, the exact relationship is unknown. Depending on what area of study one is affiliated with, cognition and language could be separate but related or intertwined functions (speech language pathology), or language is an aspect or domain of cognition (neuro- or cognitive psychology). For the purpose of this study, language will be considered a domain of cognition, just like memory, executive functioning, attention, information processing and visual perception.

The neuropathogenesis of HIV-associated neurocognitive disorders reported in HIV and AIDS individuals have been likened to those observed in individuals with various brain pathologies such as Parkinson's disease (Green et al., 2002; Marinus et al., 2003), Huntington's Chorea (Panegyres, 2004) and mild traumatic brain injury (Murdoch & Whelan, 2009). Individuals may exhibit relatively intact language abilities on formal or "straight" linguistic tasks that rely on left hemisphere damage (found in aphasics) such as naming and object recognition (Code & Lodge, 1987), but may exhibit difficulty with more higher level linguistic language skills that interface with other cognitive processes such as attention, information processing, memory, visual spatial and executive functions. Examples of higher level linguistic abilities include semantic and phonemic fluency, verbal expression, story retelling, correction of phonologic, syntactic and semantically anomalous sentences, and anomaly detection or sentence disambiguation (Bayles & Boone, 1882; Longworth, Keenan, Barker, Marslen-Wilson and Tyler, 2005).

Hence based on the interdependence of cognition and language, cognitive-linguistic abilities would include attention, memory, executive functions, visual spatial skills and language. This then implies that neurocognitive deficits can give rise to cognitive-linguistic deficits. Thus from this point on HIV-associated neurocognitive disorders and cognitive-

linguistic deficits will be used interchangeably depending on the studies being discussed, be they from the discipline of neuropsychology or speech language pathology.

An important point to consider is that individuals with HIV and AIDS can exhibit difficulties on straight serial linguistic tasks particularly if they present with HIV-associated dementia – the severest of HIV-associated neurocognitive disorders. So far the literature review has only alluded to the cognitive-linguistic skills being subserved by cortical-subcortical neuronal circuitry. How cortical-subcortical circuitry can influence cognitive-linguistic functioning is discussed below.

2.6. 4 Evidence for cortical-subcortical functioning.

Early researchers on cognition viewed cognition as a horizontal or lateral activity of the cortex (Koziol & Budding, 2009). In other words, they took a cortico-centric view or locationist view of cognition. They stated that cognition and language were controlled in the cortex and specific locations of the cortex were responsible for certain cognitive and linguistic processes. The sub-cortical structures such as the basal ganglia and cerebellum were relegated to the co-ordination of movement. The basal ganglia was associated and still is associated with either hyperkinetic or hypokinetic movement disorders observed in Huntington's and Parkinson's diseases (Duffy, 2005; Freed, 2000). These pathologies are characterized by a general loss of voluntary control of movement in that there is either too much or too little movement, essentially resulting in the loss of intentional control over movement.

According to Koziol and Budding (2009), this view of compartmentalizing functions of cognition and motor is too simplistic because it offers a false sense of security in the

understanding of brain-behaviour relationships. For example many regions of the posterior cortices participate in somatosensory functions and a substantial region of the frontal lobe participates in motor functioning. Hence, if the cortex plays a role in non-cognitive functioning surely the same can be considered of the subcortex.

Due to advances in imaging techniques such as fMRI, positron emission tomography (PET), computed tomographic (CT) scans and physiological techniques such as cell recording and neuronal tracing, substantial evidence for promoting the involvement of subcortical structures in cognitive and language processes is now emerging. Researchers such as Longworth et al., (2005), McCabe, Sheard and Code (2008), Melrose, Tinaz, Boer Castelo, Courtney and Stern (2008), Murdoch and Whelan (2009), and Woods et al.(2004) are now proposing a vertical or fronto-striatal approach to studying disorders of cognition and language. For example, in Huntington's disease, it is not uncommon to observe changes in executive functioning as the initial signs of the disorder. Huntington's disease is characterized by a motor incoordination and patients with this diagnosis commonly demonstrate cognitive deficits in working memory, set shifting and decreased information processing (Koziol & Budding, 2009). Furthermore, patients with posterior and inferior involvement of the cerebellum can also present with cognitive deficits instead of motor disturbances (Ito, 2008; Houk and Mugnaini, 2003; Schmahmann & Caplan, 2006; Schmahman & Pandaya, 1997; and van Mier and Petersen, 2002).

Technological advances have also significantly improved our understanding of neuronal structures, their connective patterns and how structures relate to cognitive functioning. Neuronal connections between regions of the cortex and basal ganglia, and discrete circuitries between these areas of the neocortex and the cerebellum have been identified. These neuronal networks provide the anatomic substrate for supporting not only

motor, but also cognitive and language functions (Middleton & Strick, 2000). The circuits originate in the cerebral cortex. After passing through the various subcortical structures within the straitum, the circuit re-enters the cortex and terminates very near the same region in which the circuit originated (Koziol & Budding, 2009). Therefore a general feature of these circuits is a cortical-subcortical-cortical loop of interaction. Within the nervous system loops of interaction of this type are considered to have a modulatory function. This implies that cortical-subcortical circuits regulate or modulate neural impulses thus changing the nature of input received from various cortical domains.

Subcortical regions of the brain refer to structures positioned deep within each cerebral hemisphere, beneath the level of the cortical mantle. These structures include the basal ganglia (straitum), internal capsule, thalamus, brain stem and the cerebellum (Murdoch & Whelan, 2009). For the purpose of this study, only the fronto-striatal (basal ganglia) circuitry will be discussed because of the role it plays in mediating neurocognitive processes observed in HIV-associated neurocognitive abilities or cognitive-linguistic abilities. It is important not only to understand what HIV-associated neurocognitive disorders are but also how they are determined or assessed in order to monitor the neurotoxicity of HAART and also disease progression because HIV-associated neurocognitive disorders have been shown to significantly correlate with mortality (Heaton et al., 2010; Wilkie et al., 1998). Hence this study serves to highlight the significance of providing a reliable and time-efficient mode of assessing HIV neurocognitive disorders or cognitive-linguistic abilities in the context of a resource-limited country such as South Africa.

2.7 Assessment of HIV-Associated Neurocognitive Disorders

2.7.1 Introduction.

Most of what is known about HIV-associated neurocognitive disorders has been accomplished via neuroimaging techniques and neuropsychological testing. This section describes the different methods of assessment used and the risk factors that predispose HIV-infected individuals to HIV-associated neurocognitive disorders. This section also provides a description and rationale for the assessment tools utilized in this study to assess the severity of cognitive-linguistic impairments and how they affect activities of daily living. The diagnosis of HIV and AIDS-related dementia (HAD) and minor cognitive motor disorders (MCMD) are usually made by neurologists and psychiatrists who carefully rule out alternative diagnoses.

The preceding sections have laid the foundation for assuming that individuals living with HIV and AIDS in South Africa will most likely present with HIV-associated neurocognitive deficits because of the high prevalence of HIV infection in South Africa. We know that HIV and AIDS is closely linked to poverty, so we can presume that most individuals will initiate HAART fairly late in the course of the disease because they will be accessing HAART from government public hospitals or clinics which usually initiate HAART in the later stages of the disease. We also know from neuroimaging studies that the HI virus crosses the blood brain barrier almost immediately after infection - during the asymptomatic phase. Hence if the majority of HIV-infected South Africans are accessing HAART during the latter stages of HIV and AIDS, it can be assumed that brain degeneration is occurring, albeit at different rates because of risk factors that could be influencing the presence of HIV-associated neurocognitive disorders or cognitive-linguistic impairments.

2.7.2 Biomedical Assessments.

The most useful tests in diagnosing neurocognitive deficits include neuroimaging, cerebrospinal fluid (CSF) examination, metabolic and or toxicology screen, and formal neuropsychological testing. Neuroimaging is usually an essential component of the evaluation of patients with HIV and AIDS and CNS dysfunction, including those with suspected neurocognitive impairments. Principally, it is used to detect evidence of brain injury and other pathological processes such as the mass lesions of primary CNS lymphoma or the ependymal signal changes of CMV encephalitis (Price, 1998). It can also detect abnormalities associated with HIV-associated dementia (HAD). In addition, anatomical imaging, including both computed tomographic (CT) scanning and magnetic resonance imaging (MRI), have been successful in diagnosing HAD (Berger et al., 2000) via volumetric measures (Alyward et al., 1995).

Other methods of neuroimaging that have been successfully used to investigate the brain pathogenesis of mild cognitive motor disorder (MCMD) and HAD include positron emission tomography (PET), proton magnetic resonance spectroscopy (^{1}HMRS), diffusion tensor imaging and computational anatomy techniques that reveal systematic patterns of brain changes, e.g. 3D mapping (Thompson et al., 2006). ^{1}HMRS has shown sensitivity in detecting early changes in patients with mild cognitive motor disorder, and differentiating these patients from more advanced HAD (Jarvik et al., 1993) by using neuroimaging markers that are sensitive to the metabolites in brain cells especially glial cells such as choline-containing compounds and myo-inositol (Ernst et al., 2003).

Blood-oxygen-level–dependant (BOLD), functional MRI studies have shown that regional brain activity decreases within areas commonly associated with simple attention and memory tasks in HIV-positive patients (Chang et al., 2004; Ernst et al., 2003). The results of

BOLD studies have revealed reduced efficiency in the attentional and memory networks and the recruitment of additional neural networks to compensate for the disruption of attentional networks. Another novel MRI technique, arterial spin labelling (ASL), has been used to study baseline cerebral blood flow and results have revealed that resting cerebral blood flow is inversely correlated with neurocognitive impairment (Cholewińska & Szymańska, 2009) . Measurements of cerebral blood flow to the caudate nucleus of HIV patients with varying neurocognitive performances have revealed a significant decrease in blood perfusion or flow that correlates with neurocognitive impairment (Ances et al., 2006). Routine cerebral spinal fluid (CSF) examination via lumbar puncture is the most useful in differential diagnosis rather than in directly supporting mild cognitive motor disorder (MCMD) or HIV-associated dementia (HAD), considering that findings in these patients are unspecific, that is, patients may not consistently exhibit the same make-up of white blood cells and protein (Cholewińska & Szymańska, 2009; Price, 1998).

2.7.3 Neuropsychological Assessments

In the pre-HAART era, higher CSF viral loads correlated with lower scores on neuropsychological tests with individuals with more advanced HIV disease. However, since the introduction of antiretroviral treatment, CSF viral loads have become a less reliable marker because individuals usually attain undetectable HIV-1 viremia values by current clinic assays (Cholewińska & Szymańska, 2009). Multimodal neuroimaging will thus play an increasing role in further understanding the neurobiology of HIV-associated neurocognitive disorders. Despite the accuracy of neuroimaging and cerebrospinal fluid (CSF) examination, these methods of assessment are expensive and sometimes time-consuming for resource-limited developing countries such as South Africa where long queues are the norm in order to access

treatment for HIV and AIDS and for the diagnostic equipment necessary to run neuroimaging techniques.

Formal neuropsychological testing has provided the principal endpoint measure for clinical trials of HIV-associated neurocognitive disorders and antiretrovirals (Price, 1998). Performance on such tests is not diagnostically specific, and individual test performance is variable and can be affected by a variety of factors (age, education, prior drug or alcohol use, head injury, etc.). However, if test performance is compared to appropriate norms and carefully interpreted in the particular clinical context, formal examination can help to determine whether symptoms truly reflect abnormal neurological function, and whether the character of such dysfunction conforms to that of mild cognitive motor deficits or HIV-associated dementia (Ellis et al., 2007).

In most cases, especially in under resourced medical settings as found in developing countries such as South Africa, the only method of assessing neurocognitive deficits is via neuropsychological testing. The role of neuropsychological assessment is to probe different cognitive domains and abilities such as learning, recall, attention, executive functions or perceptual motor skills in individuals after brain dysfunction related to trauma, disease, psychiatric/neurological disorders or general medical conditions (Franzen, 2000). It is important to remember that there is no perfect test that corresponds exactly to a putative cognitive ability.

Within the area of HIV and AIDS research, neuropsychological assessment seeks to identify cognitive strengths and weaknesses with regard to treatment planning or monitoring as well as identification of the early symptomatology of HIV-related cognitive deficits (Orr & Pinto, 1993). Some discussion has ensued advocating greater reliance on neuropsychological test results to categorize asymptomatic, mild, moderate and severe impairment rather than

using diagnostic categorization (Corless et al., 2000). This view is supported by the knowledge that mild impairments can be predictors for HIV disease progression, mortality and poor medication adherence (Dawes & Grant, 2007; Heaton et al., 2010; Valcour & Paul, 2006; Wilkie et al., 1998).

2.7.4 Rationale for neurological assessments.

In essence neuropsychological tests are better suited for use in developing counties than expensive neuroimaging techniques for several reasons. Firstly, they are cheaper to use and can assess more individuals in a given timeframe whereas neuroimaging techniques are quite expensive. Secondly, patients are less likely to sit and wait in long queues to be assessed. Furthermore, neuropsychological tests are better at determining the severity of HIV-associated disorders than neuroimaging techniques. Neuroimaging methods can detect and observe the brain injury and mechanisms of brain injury but not necessarily inform on the severity of HIV-associated neurocognitive disorders. It is important to know the severity of HIV-associated neurocognitive disorders because it serves as a good indicator of disease progression, mortality and drug adherence (Dawes & Grant, 2007; Heaton et al., 2010; Valcour & Paul, 2006; Wilkie et al., 1998).

Moreover, in resource-stricken environments such as those found in most areas of South Africa, there is a shortage of trained health personnel. It is usually the neurologist and psychiatrist who diagnose mild cognitive motor disorders and HIV-associated dementia and they are not always on hand to diagnose HIV-infected individuals who might exhibit neurocognitive disorders. So the versatility of neuropsychological tests in developing countries such as South Africa lies in the fact that neuropsychological tests can be administered by other

allied health professionals such as speech language pathologists, neuropsychologists, cognitive psychologists and occupational therapists.

Screenings such as the Mini Mental State Exam can be administered by nurses. Assessment by other professionals allows for HIV-infected individuals to receive appropriate referrals and treatment. The aim of citing the advantages of neuropsychological testing in developing countries is not to negate the importance or usefulness of neuroimaging methods in South Africa, but to highlight the utility of conducting neuropsychological testing in developing countries where neuroimaging methods are not accessible to the majority of the population.

Most comprehensive neurological tests have proven to be expensive, time-consuming to administer and cumbersome and taxing to perform for patients at bedside or in a clinical setting. As a result, shorter tests and screening tools have been developed to diagnose HIV-associated neurocognitive disorders including HIV-associated dementia (HAD). Although not a substitute for more comprehensive neuropsychological assessment, shorter tests or screening tools have yielded valuable information that significantly correlated with information obtained from more comprehensive tests (Struss, Meiran, Guzman, Lafleche & Willmer, 1996). These shorter tests and screening tools have been found to be just as accurate as long tests in accurately diagnosing HIV-associated neurocognitive disorders including HIV-associated dementia (Struss, et al., 1996) and cognitive-linguistic disorders. Therefore, for the purpose of this study the Cognitive Linguistic Quick Test was utilized.

Rationale for the Cognitive Linguistic Quick Test

The Cognitive Linguistic Quick Test (CLQT) is a standardized test that was developed to assess the cognitive and linguistic functions of adults (18-89 years old) with suspected neurological dysfunction caused by degenerative diseases such as Alzheimer's dementia, or vascular conditions such as strokes, or brain damage such as traumatic brain injury (Helm-Estabrooks, 2001). The Cognitive Linguistic Quick Test was developed in the United States of America in 1999 and normed on English- and Spanish-speaking adults who presented with stroke, traumatic brain injury and dementia. The CLQT allows for the assessment of the five domains of cognition, namely attention, memory, executive functions, language and visual spatial skills.

The five domains are assessed through ten tasks, which include personal facts; symbol cancellation, confrontational naming, clock drawing, storytelling, symbol trails, generative naming, design memory, mazes and design generation (refer to Appendix V). These ten tasks are modifications or adaptations of reputable tests used in neuropsychology and speech language pathology. Even though the test is called "quick" it is not as brief as a screening measure that is narrow in focus and does not cover many cognitive domains such as the Mini Mental State Examination. As a test it is very versatile in that it can be used across disciplines such as speech language pathology, neuropsychology and cognitive psychology.

Although the test was not normed on individuals with Parkinson's disease, it was successfully utilized to determine the cognitive and linguistic abilities of patients with Parkinson's disease (Parashos, Johnson, Erickson-Davies & Wielinski, 2009). Parkinson's as a disease is very similar to HIV and AIDS in that it is neurogenic and degenerative in nature. It involves the CNS, particularly the brain, and is degenerative in that the disease gets progressively worse until the person becomes debilitated and reliant on others for care. The

neuropathogenesis of Parkinson's disease is also very similar to HIV and AIDS. Despite the fact that it is generally agreed that Alzheimer's disease, Parkinson's disease and HIV and AIDS are different conditions, they form part of a neuropsychological homogeneous group in that they are neurogenic and degenerative in nature.

Hence the test was deemed suitable to use with individuals with HIV and AIDS even though the Cognitive Linguistic Quick Test has not yet been normed on HIV-infected individuals. This test was also found to be suitable for use with HIV-positive individuals because the objective of the Cognitive Linguistic Quick Test (CLQT) is to assess higher order linguistic skills that are reliant on the domains of attention, memory, visual spatial skills and executive functions. Moreover, the intent of the CLQT is aligned with the purpose of this study which was to investigate how the cognitive linguistic abilities of individuals living with HIV and AIDS are influenced by HAART.

The CLQT was standardised primarily on a white population with African Americans and Hispanics (of South American descent) (Helm-Estabrooks, 2001**).** The average education levels included 13 to 15 years of education, though the clinical studies included individuals who had less than 12 years of education. So in effect, people taking the test do not need a high school education because half of the tasks in the test do not have high language demands (Helm-Estabrooks, 2001**).** This was done to assist in evaluating the cognitive functions of examinees who exhibit language deficits. The CLQT has not previously used in assessing cognition and linguistic functions in adults living with HIV. The standardized population was very different from the HIV population utilized in this study, which was predominantly black African, with less than 12 years of education, coming from a low socioeconomic background.

Normatives for the CQLT have been conducted on English- and Spanish-speaking adults, but the participants in this study were English, Sotho, Tswana or Zulu speakers.

However, this test was deemed suitable for this population based on the findings conducted from a pilot study pertaining to this research. The CLQT was able to identify clear deficits in all five cognitive domains, as reported in the literature using more expensive, elaborate and time-consuming neuropsychometric evaluations (e.g. Berghuis, Uldall & Lalonde, 1999; Savage, Jackson & Sourathathone, 2003). This suggests that the CQLT is an appropriate instrument for use in the initial investigation of cognitive deficits in patients with HIV or AIDS in South Africa (Mupawose & Broom, 2010).

Moreover, it is well documented that HIV and AIDS patients present with both cortical and subcortical degeneration, and thus the tasks on the CQLT were deemed suitable for assessing this. For example, tasks include verbal fluency, design generation, symbol trails, symbol cancellation, clock drawing, and mazes which are all reliant on working memory. It has been suggested that working memory is mediated by fronto-striatal networks. Working memory is a subsystem of short-term memory, which allows the retention of information for brief periods (Baddeley, 1987, 2003). Working memory can be more simply defined as the ability to hold information cognitively "on line" for a brief period of time, temporarily, but sufficiently long enough for task completion (Koziol & Budding, 2009). It allows the individual to plan and organize higher order behaviour which is characterized by a division of labour between maintaining information "on line", which is a function of the cortex, and updating information which is "gated" by the basal ganglia. This may also explain why some patients who exhibit neurocognitive deficits perform relatively well on functional everyday activities such as communication of needs and wants, and activities of daily living, but demonstrate difficulties learning or adding new to information already "on line" (Koziol & Budding, 2009). This research assumes that the HIV-associated neurocognitive disorders and cognitive-linguistic functions are underpinned by fronto-basal ganglia networks. The

Cognitive Linguistic Quick Test (CLQT) thus met all the assumptions and premises of the study.

Description of the CLQT.

As previously mentioned, the CLQT is composed of ten tasks, which include personal facts, symbol cancellation, confrontational naming, clock drawing, storytelling, symbol trails, generative naming, design memory, mazes and design generation. These ten tasks collectively assess five domains: attention, memory, executive functions, visual spatial and language. Following is a brief description of cognition and the five domains under investigation.

Cognition as a general term refers to stored knowledge and the process for making and manipulating knowledge (Bayles & Tomoeda, 2007). According to Helm-Estabrooks (2001), attention is "multifaceted, multisensory behaviour that interacts with other cognitive processes and is essential to the performance of all daily and clinical tasks'' (p. 3). Attention is one of the cognitive areas most affected by the HI virus as the disease process progresses.

Memory is not a single entity but rather a complex process. Without memory there would be no meaningful cognition as we know it. The ability to access memory stores enables us to interpret our ever-changing environment, modify behaviour to ensure survival and lesser objectives (Bayles & Tomoeda, 2007). There are three main divisions in memory functioning and these include working memory, learning and encoding, and recall. Working memory is utilized when information is required to be manipulated and processed (Baddeley, 2003; Koziol & Budding, 2007). It is sometimes linked to attentional resources and is an active memory function, as the person actively concentrates on remembering and manipulating information. This type of memory is usually measured by tasks of arithmetic, or memory for

number strings and words. The second part of memory, long-term memory, is the learning and encoding of information into mental representations that are able to be retrieved into conscious awareness at a later time that is called remembering.

Encoding refers to the transfer of information into mental representations (Panegyres, 2004; Lozito & Mulligan, 2006). The ability to learn is process of being able to recall or retrieve information (mental representations) that has stored in long term memory, and this is a function of working memory (Owens, 2004).Executive function is another construct of cognition and is a measure of a person's ability to essentially self-regulate and direct their own behaviour, and which is made up of many subparts (Lezak, 1995). These subparts include the ability to make informed choices, planning and being able to act purposively and effectively (Sbordone, 2000). Within the domain of executive functioning, researchers have identified impairments in inhibition (Hinkin, Castellon, Hardy, Granholm & Siegle, 1999), set shifting (Woods et al., 2004), manipulation within working memory (Dawes & Grant, 2007), planning and cognitive sequencing (Sahakian, Elliott, Low, Mehta, Clark and Pozniak, 1995), reasoning and problem-solving. Executive functions are said to be mediated by fronto-striatal circuitry.

Visual spatial skills "involve visual perception (the ability to scan, discriminate, analyse, recognize and interpret what we see) and construction (the ability to create visual stimuli using perceptual skills and motor responses (Helm-Estabrooks, 2001, p. 3). The ability to perceive visual information is dependent on healthy eyes without disease. Visual spatial skills are necessary to execute many clinical tasks and functional activities of daily living.

Language refers to the symbol system by which sound is paired with meaning for a particular purpose (Bayles & Tomoeda, 2007). It is a uniquely human and complex behaviour comprising the interrelated aspects of semantics, phonology, morphology, syntax and pragmatics. Language can be either expressive or receptive. Expressive language entails the

"intentional" sharing of information by means of a symbol system that can either be linguistic (verbal) or non-linguistic (gestures, sign language, graphic as in written words or pictures). Receptive language, on the other hand, is the ability to perceive and interpret (understand or process) the linguistic or non-linguistic message being expressed or shared. The ability to perceive verbal language is dependent on healthy ears free of conditions that can impede a person's ability to hear effectively.

Cognitive domains are evaluated either through clinical tests or tasks. It is both simplistic and unrealistic to assume that a task can assess only one domain. The performance of most tasks is reliant on the interaction of two or more domains. For example, the block design task requires that an individual attend to and comprehend the verbal instruction, perceive the spatial relationship among the components, form a visual spatial representation or design, be able to form different designs according to the instructions, and use motor skills to reproduce the design on paper (Broshek & Barth, 2000). Generally, all tasks require attention and receptive language to perform. While it is true that no clinical tasks call upon only one domain, the accomplishment of certain tasks is more reliant on specific cognitive domains. For example, the simple task of naming an object requires perception, access to long-term memory, association, decision-making, and motor planning in terms of speech output and self-monitoring (Bayles & Tomeoda, 2007).

Tasks on the CLQT and application to HIV and AIDS.

The ten CLQT tasks were developed by reviewing procedures and tests used to assess cognitive functions in healthy adults and in adults with neurological functions. Most of these tests have been used with individuals with HIV and AIDS in developed countries and a few

sub-Saharan African countries to assess neurocognitive functioning. A description of the tasks and similar test that have been used on individuals with HIV and AIDS follows below.

Personal facts: The purpose of this task is to assess episodic memory (personal facts), orientation to place and year, and the ability to communicate these facts through language. To perform this task the participant is required to answer four questions about their date and place of birth, current age and address (Helm-Estabrooks, 2001**).** The primary cognitive domains assessed by this task include memory (recent and long term) and language in terms of word retrieval, verbal language comprehension and expression (Helm-Estabrooks, 2001**).** It has been suggested that the deficits of language and memory are predictive of dementia (Bayles & Boone, 1982; Bayles & Tomoeda, 2007; Code and Lodge, 1987). This task can thus be found in tests such as the Mental State Questionnaire and the Ross information Processing Assessment that assess cognitive state or information processing. This sub-test is sensitive to organic-related (brain degeneration) dementia. Memory impairment observed might be due to atrophy of the hippocampus (Panegyres, 2004) as a result of neuronal loss which is known to occur early in HIV-1 brain infection, and this has been observed in fMRI studies of HIV-infected individuals (Ellis et al., 2007 ; Thompson, Dutton, Hayashi, Lu et al., 2006).

The assessment of memory is important, as it may be the initial symptom that alerts the clinician to the possibility of a brain disease (Panegyres, 2004). The presence of memory and/or orientation problems may influence new learning and functional activities. Furthermore, the hippocampus plays a pivotal role in new learning (Panegyres, 2004). It was hypothesized in this study that the participants who exhibited severe HIV-associated neurocognitive disorders would perform poorly on this subtest at baseline. Whereas those participants who performed well may not necessarily exhibit deficits in episodic memory and have HIV-associated

dementia, but may have milder forms of HIV-associated neurocognitive disorders or cognitive-linguistic deficits with other types of memory not assessed by this task.

Several tests have been used on individuals living with HIV and AIDS that assess learning and memory. Sacktor, Wong, Nakasujja et al. (2005) used the Rey Auditory Verbal Learning Test on a Ugandan sample and found that HIV-positive individuals performed worse than HIV-negative individuals on this test. Another test that has been used on HIV-infected individuals is the California Verbal Learning Test (Melrose et al., 2008). Melrose et al. (2008) found that there was a significant difference in neurocognitive performance between HIV-positive and HIV-negative individuals with the California Verbal Learning Test where HIV-positive individuals performed better. Sacktor, Nakasujja, Skolasky, Robertson, Wong et al. (2006), using the WHO-UCLA-Auditory Verbal Learning Test, observed that HIV-positive individuals living in Uganda exhibited very low mean scores for this test (indicating impairment) at baseline that improved with HAART.

Similarly, Letendre, van den Brande, Hermes et al. (2007) observed very low mean scores with the Hopkins Verbal Learning Test-revised that improved with HAART. Low mean scores were also observed by Lopez, Wess, Sanchez, Dew and Becker (1998) on the Rotary Pursuit Learning Test and correlated with self-report measures on memory abilities. Other forms of memory have also been assessed on this population such as visual and logical using the Wechsler Memory Scale (Lopez et al., 1998; Wilkie et al., 1998), Buschke Selective Reminding Test (Wilkie et al., 1998) and Figure Memory Test (Wilkie et al., 1998). Performance on all three measures indicated impaired visual and/or logical memory abilities among HIV-infected individuals.

Verbal memory has been evaluated using the Four Word Verbal Recall Test and Word Verbal Free Recall Test. Cohen et al. (2001) found verbal memory to be impaired at baseline

with the Four Word Verbal Recall Test but improved once HIV positive individuals started taking HAART. Using the Word Verbal Free Recall, Lopez et al. (1998) reported that test scores were low and correlated with self-report measures on memory abilities. Overall it would appear that HIV-positive individuals exhibited deficits in most of the memory categories and these seemed to improve when individuals started taking HAART. It is therefore vital that memory be assessed because it is critical regarding medication adherence in terms of remembering instructions on medication intake (Riepe, Riss, Bittener & Huber, 2003) and predictive of early brain degeneration (Panegyres, 2004).

Symbol cancellation: The purpose of this task is to evaluate visual attention, scanning, discrimination, inhibition and response shifting within quadrants of space (Helm-Estabrooks, 2001**).** This task entails the participants being shown a page on which abstract symbols are arranged in what appears to be a random pattern, with the target stimulus appearing three times in each quadrant of the page. Other abstract symbols (foils) are put on the page that looks similar to the target abstract symbol to increase the visual attention demands. Examinees are instructed to cross all examples of the symbol (Helm-Estabrooks, 2001**).**

The cognitive domains that are evaluated in this task are attention and visual spatial skills. This task appears to be an adaptation of the Symbol Digit Modalities Test, the Digit Symbol subtest of the Wechsler Intelligent Scales (WAIS-DS) and the Symbol Search subtest of the Wechsler Intelligent Scales (WAIS-SS) which monitors psychomotor speed, attention, visual scanning and information processing. Attention is an important cognitive skill essential to learning new information and remembering previously learnt information. Furthermore, if an individual cannot inhibit incorrect responses and appropriately shift attention, the individual will have problems with planning and problem solving.

Both the Symbol Digit Modalities Test (SDMT) and WAIS-Digit Symbol (WAIS-DS) have been used to assess neurocognitive functioning such as attention, information processing speed, visual scanning, inhibition and response shifting in individuals living with HIV and AIDS. Using the Symbol Digit Modalities Test, Sacktor, Lyles, Skolasky et al. (1999) found that HIV-positive individuals on HAART performed better than HIV-positive individuals who were on monotherapy. Cysique, Maruff and Brew (2004) found that HIV-negative individuals performed better than HIV-positive individuals on the SDMT.

However, they did notice a difference in performance between HIV-positive individuals on high CNS penetration HAART versus those on low CNS penetration. Sacktor, Nakasujja, Skolasky, Robertson, Wong et al. (2006) and Sacktor, , Nakasujja, Skolasky, Robertson, Musisi et al. (2009) showed that HIV-positive individuals living in Uganda exhibited very low mean scores for the Symbol Digit Modalities Test (indicating impairment) at baseline that improved with HAART.

Using the Wechsler Adult Intelligence Scale Revised-Digit Symbol Test (WAIS-DST), Sacktor, Wong, Nakasujja et al. (2005) found from their study conducted in Uganda that the HIV-negative individuals performed better than HIV-positive individuals. Moreover, Heaton et al. (2010) in their longitudinal study found that the neurocognitive impairments persisted even after HAART when monitored with the WAIS-DS. They also observed that impairments were related to the progression of the f HIV. Overall it would appear that HIV-positive individuals, especially if they present with severe HIV-associated neurocognitive disorders, exhibit difficulties performing symbol-related tasks that assess attention, visual scanning, response shifting tasks and these seem to improve when individuals start taking HAART.

Confrontational naming: The purpose of this task is to assess the ability to name pictures (Helm-Estabrooks, 2001**).** The task requires the participants to name ten common objects. This task evaluates the cognitive domains of language (semantics and phonology)(Helm-Estabrooks, 2001**)**. The ability to name a picture requires the perception and recognition of the item being named and retrieval of its referent from long-term memory (Bayles & Boone, 1982), association, word retrieval, decision-making, motor planning and self-monitoring. If an individual exhibits difficulty in naming, this can be indicative of dementia. Tasks or tests of confrontational naming are most commonly used as measures of gross language skills especially in expressive language. Disruptions in language usually occur along a continuum ranging from basic units of language, such as producing sounds, to difficulty processing higher language (linguistic) skills or conversational competence (Johnstone, Holland & Larimore, 2000).

Using the Western Aphasia Battery – naming subtest, Mathew and Bhat (2008) reported that the naming abilities of their HIV participants fell within the normal range. This came as no surprise because we would expect individuals living with HIV and AIDS to perform fairly well on serial linguistic tasks that do not rely heavily on other cognitive abilities. This type of performance is typical of individuals with brain degeneration in both the cortical and subcortical regions such as seen in individuals with HIV-associated cognitive-linguistic deficits.

Clock drawing: Though this task is included in the assessment, results yielded from this task were not used to calculate domain scores. Clock drawing thus has its own rating score. The purpose of this task is to determine severity of neurological decline, especially in progressive diseases (Helm-Estabrooks, 2001**).** This task requires the integration of all five previously

mentioned cognitive domains since all the skills of sustained attention, memory, planning, abstract thinking, organization; receptive language and visual spatial skills are required. As a task it exhibits minimal ethnic and educational bias. Research has shown that this activity is a good screening indicator for dementia. Results from clock drawing have correlated well with other dementia scales such as the Mini Mental State Examination, Blessed Dementia Scale and the Global Deterioration Scale (Berger, Lutz, Frölich, Weber & Pantel, 2008; Heinik & Shaikewitz, 2009). However, there is no research to date to determine how well clock drawing correlates with dementia in individuals living with HIV and AIDS. It is assumed that there is a significant correlation between clock drawing and HIV-associated dementia tests such as the International HIV Dementia Scale. This is because of the significant correlation that has been reported between the International HIV Dementia Scale and other dementia scales such as the Mini Mental State Questionnaire (Ciccarelli et al., 2011) and the Karnofsky Performance Scale (Sacktor, Wong, Nakasujja et al., 2005).

Story telling: The purpose of this task is to determine the ability of participants to recall verbal information in the form of a story (Helm-Estabrooks, 2001**).** This task is made up of two components. The first entails the examiner reading aloud a short story with many details and the participant retelling the story including all the important details (Helm-Estabrooks, 2001**).** The second part involves the participant answering yes/no questions about the story. The cognitive domains being evaluated are attention, memory (verbal working memory) and language (language comprehension and production) (Helm-Estabrooks, 2001**).** The ability to retell a story depends on an individual's capacity to store new information in the long-term memory for subsequent retrieval (Bayles & Boone, 1982) and also to retain information in working memory for a short period of time (Hem-Estabrooks, 2001). Bayles and Boone (1982)

have suggested that difficulties in story telling are also predictive of the early stages of dementia. Heaton et al. (2010) used this task with individuals living with HIV and the results revealed that performance on this task was associated with HIV disease progression. Those individuals with the worst disease progression performed most poorly that higher CD4 counts. This implied that verbal working memory which is mediated by fronto-striatal circuitry progressively deteriorates as the disease progresses.

Symbol trails: The purpose of this task is to assess working memory, planning and mental flexibility without placing a demand on language (Helm-Estabrooks, 2001**)**.. The task requires an individual to connect shapes, alternating between circles and triangles in order from smallest to largest. The main cognitive domains being evaluated here are attention, executive functions and visual spatial skills (Helm-Estabrooks, 2001**)**. To be able to carry out this task one needs a measure of concentration and attention and planning, as well as mental flexibility which are all essential for everyday problem-solving (Helm-Estabrooks, 2001**).**These processes have been noted to be affected in the latter stages of HIV-associated neurocognitive disorders (Dawes & Grant, 2007; Fernandez, 2005). This task is an adaption of the Trail Making Test – Parts A and B, and Colour Trail Making Test.

Both these tests have been used on individuals with HIV and AIDS to assess attention, executive functioning and visual spatial skills. Ciccarelli et al. (2011) using the Trail Making Test – Part B described the HIV- positive individuals as performing better on this test than HIV-positive individuals. Moreover, there was a difference in performance between those individuals on low versus high CNS-penetrating antiretrovirals. Heaton et al. (2010) reported that performance on the Trail Making Test (A and B) was associated with HIV and AIDS disease severity and co-morbid conditions. Those individuals with the worst disease

progression performed the poorest. Furthermore, the impairments persisted while on ARVs. Singh et al. (2010), using the Trail Making Test (Parts A and B), found that HIV-positive participants in South Africa performed poorly on this test. The Colour Trail Making Test appears to have yielded similar results. Cohen et al. 2001 reported impaired abilities with the Colour Making Test at baseline and that continued to improve the longer the person remained on HAART. Their non-HAART group which consisted of participants taking monotherapy performed worse than those who were prescribed HAART. Sacktor, Wong, Nakasujja et al. (2005) in their study in Uganda stated that the HIV-negative individuals performed better than HIV-positive individuals on the Colour Making Test. Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al. (2009) further observed that HIV-positive individuals who presented with impaired abilities at baseline improved while on HAART.

Generative naming: The purpose of this task is to evaluate a person's ability to generate exemplars both semantically and phonemically (Helm-Estabrooks, 2001**).** This task is done in two parts. Firstly, the participants are required to generate as many items as possible belonging to a semantic category. After that they are required to name as many items starting with the letter "m" (phonemic fluency) (Helm-Estabrooks, 2001**).** This task specifically targets working memory, language and executive function. Generative naming or semantic fluency is a semantic process that taps into the cognitive functions of working memory, language, executive functions specifically organization (categorization) (Helm-Estabrooks, 2001**)**.

This task can show up disruption in fronto-striatal processing, especially if an individual exhibits difficulties generating phonemic exemplars (Koziol & Budding, 2009). The task of performing a phonemic fluency task is cognitively more difficult because the

brain does not store words according to letters but according to semantic categories (Ross, 2003; Salmon & Chan, 1994). So an individual has to develop a new strategy for retrieving words different from those that are semantically stored (Koziol & Budding, 2009). Therefore, when a person does well on category fluency and poorly on letter fluency this does not constitute a specific retrieval problem. Instead this implies fronto-striatal involvement (Woods et al., 2004). Lastly, the area of verbal fluency is often more affected than other linguistic abilities, like naming, comprehension and reading lending additional support for a pattern of fronto-striatal deficits (Koziol & Budding, 2009).

Design memory: The purpose of this task is to assess the working/immediate visual memory with minimal language demands (Helm-Estabrooks, 2001**).** This task requires participants to recall and point to designs that match the two target designs. The cognitive domains under investigation here are attention, visual memory and visual spatial skills (Helm-Estabrooks, 2001**).** It has been suggested that individuals who exhibit HIV-associated neurocognitive deficits may present with difficulties learning new information which is an aspect of higher order control, automatic processing and instrumental and incidental learning, especially if they have been further diagnosed with HIV-associated neurocognitive disorders (Fernandez, 2005; Koziol & Budding, 2009; Larson, 1998;). Other tests similar to this task that have been used on individuals living with HIV and AIDS include the Figure Memory Test (Heaton et al., 2010) and the Rey Figure Recall Test (Ciccarelli et al., 2011; Cysique, Maruff, Barby et al., 2006).

Using the Figure Memory Test, Heaton et al. (2010) reported that performance on this test was associated with HIV and AIDS disease severity and associated conditions. Ciccarelli et al. (2011) observed in their cross-sectional study that HIV-seronegative individuals performed better on this test than HIV-positive individuals. It has been postulated that deficits

in attention and visual working memory are caused by disruptions in the fronto-striatal circuitry (Koziol & Budding, 2009; Woods et al., 2004), and we know that brain lesions occur both in the cortical and subcortical areas of the brain in HIV-infected individuals. Therefore it is not surprising that HIV-positive individuals performed worse than HIV-negative individuals.

Mazes: The purpose of this task is to assess executive functions while placing minimal demands on language (Helm-Estabrooks, 2001**).** In this task the examinee must plan a course of action, reject or inhibit incorrect choices, and any mistakes they make. This test also helps to assess attention and visual spatial skills (Helm-Estabrooks, 2001**).** This task was adapted from the Wechsler Intelligence Scales III – mazes subtest. "A high score suggests good planning abilities that involve both maintaining a flexible mental set and impulse control. In contrast, a low score indicates poor visual motor coordination and impulsivity. Low scores may also reflect poor planning, sequencing and monitoring behaviour" (Groth-Marnat, Gallagher, Hale & Kaplan, 2000, p.180). These executive function deficits are often indicative of fronto-striatal circuitry disruptions. Interestingly, Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al. (2009) in their longitudinal study in Uganda using HIV-positive individuals found that executive functions showed the most significant improvement compared to the other cognitive domains under investigation. This could have been due to the fact that executive functions responded better to HAART.

Design generation: The purpose of this task is to assess the executive functions of productivity and creativity (Helm-Estabrooks, 2001**).**. Participants are asked to draw four straight lines to connect four dots to make a unique design. This test also helps to assess

attention and visual spatial skills (Helm-Estabrooks, 2001**.** To perform this task a person needs to be able to self-monitor and avoid preservations, a behaviour that has significant negative impact on functional actions. In addition, creative and productive thinking even when language is impaired is a skill that is crucial to communicating in unpredictable, everyday situations (Helm-Estabrooks, 2001). This task was adapted from the Wechsler Adult Intelligence Scale Revised – Block Design where patients have to generate designs and match designs (Groth-Marnat et al. 2000). In this test "high scores indicate good non-verbal concept formation, excellent capacity for visual spatial organisation, good concentration, and fast visual motor speed. Low sores may suggest difficulties working with visual spatial materials, problems with sustained or perceptual problems" (Groth-Marnat et al., 2000, p. 172). Wilkie et al. (1998) used the Wechsler Adult Intelligence Scale Revised – Block Design (WAIS – BD) subtest in their longitudinal study with 119 HIV-positive males. This test showed significant impaired cognitive abilities among the HIV positive males.

When HIV-positive individuals were compared to HIV seronegative individuals their performance was poorer across all five cognitive domains. Therefore, neuropsychological testing provides an estimate of the individual's best cognitive performance within an isolated, time-limited context. However, this performance may be unrepresentative of the on-going demands faced in everyday situations especially in individuals with relatively mild changes in their cognitive-linguistic abilities (Warriner et al., 2010). As a result, a self-reporting interview schedule was incorporated in this study to compliment the findings of the Cognitive Linguistic Quick Test. The aim of this survey was to determine whether cognitive-linguistic abilities can affect activities of daily living, since the CLQT could only provide information on the impairment.

A summary of studies that have been conducted to investigate the presence of HIV-associated neurocognitive disorders and the effects of HAART are presented in Table 2.8

Table 2.8 Summary of HIV-Associated Neurocognitive Disorders Studies in both Developed and Developing countries.

Authors	Country	Sample (N)	Measure	Cognitive domain	Findings
Lopez et al. 1998	USA	72 HIV+ Mixed gender w/ more males On HAART Longitudinal	WAIS WMS COWAT NART WVFRT TMT A TMT B RPLT SRSS (functional)	Memory Language Exec.function Visuospatial	Self-reported scores correlated with severity of HIV, depression, cognitive and neurological complaints Complaints of specific cognitive deficit reflected overall slow processing speed and psychomotor speed.
Cohen et al. 2001	USA	23 HIV+ Females On HAART Comparison Grp 70 HIV+ Non HAART Longitudinal study	GPB CTMT COWAT FWL No functional assessment	Psychomotor Memory Language Exec.function	Baseline performance the same. HAART group improved overall than non HAART grp HAART did not influence memory More improvement noted at 18 months than 12 months or on HAART
Woods et al. 2004	USA	30 HIV – 72HIV+ Gender mixed with more males On HAART	COWAT	Language	HIV+ with dementia performed worse than HIV+ without dementia and HIV- No difference in performance between HIV+ non demented and HIV - Findings support fronto-striatal damage
Sacktor et al. 2006	Uganda	23 HIV + Longitudinal Gender mixed w/ more females No comparigrp On HAART after baseline measure	IHDS AVLT GPB SMDT CTMT WAIS-DSF WAIS-DSB KPS (QOL)	Memory Psychomotor Visuospat Exec. Funct Attention	Mean changes seen for each test. Signif. Improvement in verbal memory, psychomotor and exec. Functioning. HAART improves HIV-associatedneurocog disorders including dementia Functional

					improvement over time from impaired can't work to total independence
McCabe et al. 2008	USA	2 HIV + male 1 HIV- Longitudinal HAART?	BNT Token Test RHLB-metaphor RHLB – semantic test VF Pragmatic - Protocol WAB No functional assessment	Language Exec. function Memory Attention	HIV + dementia performed worse than HIV+ no dementia. Control did better than HIV+ non dementia and HIV + dementia exhibited Pragmatic probs Intact serial linguistic tasks-no probs on WAB Failed letter fluency, metaphor intepretation
Cysique et al. 2009	Australia	37 HIV+ Longitudinal	GPT PASAT TMT A TMT B LF No functional assessment	Language Attention Pyschomotor Exec.function Infor.processing Attention	Some individuals improve at 12 weeks, but more (41%) improve at 24, 36, and 48 % after HAART initiation. Improvements greatest with those with lowest baseline performance. Improvement associated with HIV plasma load Rel. ship between improvement and HAART adherence
Sacktor et al. 2009	Uganda	102 HIV + 25 HIV- On HAART Longitudinal	IHDS AVLT GPB SDMT CTMT WAIS-DSB WAIS –DSF KPS	Memory Pyschomotor Visual spatial Exec.function ADLs – functional assessment	Impairments improved Better improvement observed in Exec. funct CD4 counts increase Improved in overall functioning HIV- generally performed better, with minimal improvement in performance Stavudine based HAART caused peripheral neurotoxicity

Singh et al. 2010	South Africa	110 HIV+ Gender mixed w/ more females Cross sectional Not on HAART	IHDS WAIS-DSF WAIS-DSB TMT- A TMT – B No functional assessment	Attention Infor.process Exec. Funct Visuospatial Psychomotor	Age and gender (though inconsistent) affected performance. Education did not affect performance Performance on all tests were impaired.

2.7.5 Psychosocial Aspects.

Since the advent of HAART many individuals infected with HAART are living and coping with HIV as a chronic illness. Frequent complaints of persistent fatigue, cognitive impairments and psychiatric illness, especially anxiety and depression, impose functional limitations on everyday activities and adversely impact quality of life (Warriner et al., 2010). Individuals on HAART are feeling better and they are living longer with the diseases and conditions that accompany a diagnosis of HIV and AIDS such as HIV-associated neurocognitive disorders or cognitive-linguistic disorders. Nevertheless, neurocognitive deficits have not dissipated with the advent of HAART and are in fact on the increase (Heaton et al.2010). Due to HIV and AIDS being a chronic condition, a person diagnosed with HIV and AIDS and exhibiting neurocognitive disorders can be considered to be disabled (Lawthers, Pransky, Peterson and Himmelstein, 2003). Hence the structured interview schedule was included in this study – to determine whether cognitive – linguistic impairments had a significant influence on an individuals' ability to conduct activities of daily living.

According to the World Health Organization there is a framework that can be applied to health states and conditions (in this case HIV-associated neurocognitive disorders/cognitive-linguistic deficits). This framework is called the International Classification of Functioning, Disability and Health (ICF) (WHO, 2002, 2005). The ICF is a framework that defines health-related states, disability and their consequences in multiple

dimensions. In addition the ICF allows health professionals across all disciplines to provide integrated assessment and intervention using a unified and standard language beyond the clinical setting.

At the inception of the ICF in 1980 by the World Health Organization (WHO) health conditions and disability states were grounded in the medical model and used the terms "impairment", "disability" and "handicap" to describe individuals. In other words, they looked at how body structure and function were impairing an individual's ability to perform an activity. However, in 2001 the ICF was revised to include aspects of the social model of health that views disability as a part of life and validates and necessitates the inclusion of a person's social and personal environment (WHO, 2001). The current version of the ICF integrates the biopsychosocial perspectives of health. The ICF in its current form comprises two parts that include functioning and disability on the one hand, and contextual factors on the other. Part I consists of body structures, body functions, activity and participation. Part II includes contextual and personal factors.

Components of the international classification of functioning, disability and health (ICF).

Part I, describes health from the perspectives of the body, the individual and society. It also includes the components of body structures and body function. Body structures refer to the anatomical parts of the body (WHO, 2002). In the case of neurocognitive deficits, the anatomical body structures involved includes the central nervous system, specifically the regions of the brain and cranial nerves due to the diffuse damage caused by the HI virus. Impairments in body structures results in impairment in body function. Body functions describe "the physiological functions of body systems" (WHO, 2002, p. 10). Aspects of impaired neurocognition within the body function would include deficits in memory, attention, visual spatial, executive function and language. Once an individual's level of

impairment has been determined, it is important to consider how these impairments impact on activities and participation in the environment.

Activity is the execution of a task by an individual (WHO, 2002, p. 10), and participation encompasses how an individual participates is the environment, i.e. the social roles one engages in, for example mother, employer, employee, church member, student and so forth. Given that cognition is required for most daily activities, the impact of neurocognitive deficits (memory, attention, executive function, language and visual spatial) on functions of everyday life can be significant and limiting (Bendict, Mezhir, Walsh and Hewitt, 2000).

Similarly, participation in life situations and social roles can be affected by neurocognitive deficits. Some of these have been identified as social isolation (Fleishman et al., 2000) and loss of employment (Dray-Spira et al., 2006) as well as reduced leisure activity to mention just a few. To further illustrate how neurocognitive deficits can impair social participation, one need only take the example of employment since employment is a major factor in maintaining income levels and living conditions among patients with long-lasting chronic conditions such as HIV and AIDS. For working individuals, employment provides not only financial benefits but also may be a source of structure, social support, role identity and meaning (Blalock, McDaniel and Farber, 2002).

Unemployment rates are high among HIV and AIDS individuals despite the wide-scale diffusion of HAART. Studies in Western countries have reported high unemployment rates among people living with HIV and AIDS ranging from 45 to 65% especially among the socially vulnerable populations (Dray-Spira et al., 2006). High unemployment rates could be attributable to neurocognitive deficits, fatigue, pain, depression, apathy and accompanying conditions. Moreover, activities and participation lead to interpersonal interaction and

relationships in major life areas and in the community, as well as providing a means of interacting in social and civic life (WHO, 2002, 2005).

Part 2 of the ICF has also raised awareness of contextual factors that facilitate or impede body function as well as participation (Threats, 2007). These contextual factors incorporate both environmental and personal factors. Environmental factors "make up the physical, social, cultural and attitudinal environment in which people live and conduct their lives" (WHO, 2002, p. 10). These factors influence access to services, opportunities and information (Cruice, 2007; Lawthers, Pransky, Peterson & Himmelstein, 2003). Environmental factors relevant to neurocognitive functioning include technology, support from family, friends and health professionals, attitude from family, friends and society as a whole, availability or access to services, efficiency of systems and legislated coherent policies related to HIV-related conditions such as cognitive deficits (Lawthers et al., 2003; WHO, 2002).

There is a burgeoning industry in tools and devices to assist individuals with neurocognitive impairment such as computers, word processing, home banking and navigation devices (McLeod & Bleile, 2003). Although these resources might not be available to individuals in within some areas of developing countries due to financial and bureaucratic barriers, home or work environments could be modified to compensate for their mental abilities. Support from friends, family and health professions has been documented to assist with coping and acceptance of diagnosis (Renwick & Friedland, 1996; Vosvick et al., 2003). Unfortunately, societal attitudes towards individuals with HIV and AIDS are more often than not still negative.

There is still a lot of stigma around the disease to the extent that HIV-positive individuals often do not disclose their status to partners, family or friends. This is debilitating for individuals who present with neurocognitive deficits because, they need the support of

loved ones to assist in activities that rely upon intact cognitive abilities. The services, systems and policies relating to individuals living with HIV and AIDS especially if they suffer from neurocognitive disorders can influence the well-being of the individual in terms of availability of drugs, treatment centres and adherence to drugs (Lawthers et al., 2003). Political factors can also affect the reality of intervention for individuals with HIV and AIDS. For example, in South Africa, the nationwide roll-out of ARVs was initially delayed by political debate on what constitutes AIDS, which further resulted in unnecessary and preventable deaths.

Personal factors include the attributes of the person and the internal influences on functioning and disability (WHO, 2002). The ICF recognizes the "large social and cultural variance" (WHO, 2002) so gender, age, other health conditions, coping style, social background, education, profession and past experience which can influence how a person responds to the diagnosis and intervention provided to address neurocognitive disorders.

Rationale for Structured Interview schedule

Functional ability in terms of HIV-associated neurocognitive disorders is a topic that hasn't been discussed in any great detail in the South African body of literature. To fill this lacuna, the researcher thus included an interview schedule to her study that looked at quality of life in terms of functional performance i.e. activities of daily living. This aspect was investigated by asking questions relating to initiating and completing activities of daily living. According to Webb and Norton (2004,) it is important to assess aspects psychosocial issues for several reasons: to monitor adherence because if a patient is not functionally performing this could be due to an inability to follow the complicated drug regimen; to determine tolerance to HAART – the patient may be experiencing terrible side effects that affect their ability to functionally perform; to assist healthcare professionals in identifying

patient health changes over time and improving communication between patient and health provider.

A structured interview schedule was thus included in this research to add more depth and supplement the cognitive-linguistic data collected. The structured interview schedule included mainly closed-ended questions and a few open-ended questions. The questions were developed and adapted for the South African context from the Cognitive Symptom Checklists® developed by O'Hara, Harrell, Bellingrath and Lisicia (1993). The interview schedule was divided into two sections: demographic information and self-reported cognitive-linguistic problems (refer Appendix VII). The cognitive-linguistic problems sub-section was further divided into attention, memory, visual spatial, language and executive functions thereby tapping into "real world" functional everyday activities such as work assessment, finances, shopping, medication management, and cooking.

Difficulties in performing these particular activities of "real world" functioning have been shown to occur in the context of cognitive-linguistic abilities associated with HIV infection (Heaton et al., 2004). Specifically executive functions and memory skills such as planning, organization and abstract thinking are particularly important for successful management of household finances, particularly shopping (Gorman, Foley, Ettenhofer, Hinkin & van Gorp, 2009). In the context of this research it was deemed important to determine how cognitive-linguistic deficits interfaced with activities and participation within the framework of the International Classification of Functioning, Disability and Health (ICF). This was achieved by conducting a structured interview schedule. The survey comprised of the same cognitive-linguistic abilities as the CLQT, the difference was the interview generated responses pertaining to activities of daily living.

Studies have been conducted investigating how cognitive, psychosocial and physical factors can influence a person's ability to function in their environment (Gorman et al., 2009;

Heaton et al., 2010; Kopinsky et al., 2004; Lopez, et al, 1998; Renwick and Freidland, 1996). For instance, with regard to cognition, Lopez et al. (1998) reported that approximately 50% of their 72 HIV-infected participants indicated that they exhibited difficulty planning and organizing household tasks and recreational activities such as cleaning, cooking, hobbies and crafts. Contrary to the research results of Lopez et al. (1998), Heaton et al. (2010) found in their study that out of the 1555 HIV-infected participants, 617 reported neurocognitive deficits; and out of the 617 participants only 30% suggested that neurocognitive deficits significantly interfered with everyday abilities.

Heaton et al. (2010), nonetheless, caution about the use of self-reports by saying that they are easy to obtain but may lead to false-positive classifications (e.g. exaggerated self-criticism due to depression) as well as false-negatives due to lack of insight or avoidance of everyday situations that require abilities which have become impaired. Conversely, despite the classifications, everyday functioning must be documented as a criterion for the impact of HIV-associated neurocognitive impairment. Although these studies used self-report measures, they were cross-sectional in nature and their participants had higher CD4 counts than those reported in this study. Therefore their studies failed to provide information on the effects of HAART in relation to cognitive-linguistic abilities and the ability to perform everyday activities.

There also appears to be a relationship between the progression of the disease and an individual's ability to perform functional abilities. For example, Sacktor, Wong, Nakasujja et al. (2005) and Wong et al. (2007) conducted studies in Uganda using both HIV-positive and HIV-negative participants. These studies revealed that participants in the HIV-positive groups reported more functional impairments on everyday tasks than the HIV-negative participants. It was further reported by Wong et al. (2007) that symptomatic complaints from

those participants in stages 3 and 4 (who were in the majority) included depression (64%), memory problems (59%), headaches (59%), numbness (54%), concentration (37%) and balance problems (32%). The findings also revealed that the greater the severity of HIV-associated neurocognitive deficits, the greater the number of individuals who complained of disease-related symptoms. Regarding their functional performance as recorded on the Karnofsky Performance Scale, HIV-infected patients with and without HIV-associated dementia reported difficulties performing functional activities, with demented patients stating the worst problems. In the research study by Sacktor, Wong, Nakasujja et al. (2005) it is not clear whether participants were taking HAART, whereas in the study by Wong et al. (2007) the majority were not taking HAART. Once again both these studies were cross-sectional in nature and failed to provide information on the effects of HAART on the cognitive-linguistic abilities of the participants in relation to everyday functional activities.

Both Sacktor, Wong, Nakasujja et al. (2006) and Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al., 2009) in their longitudinal studies with HIV –positive individuals reported that HAART had a positive effect on functional performance. They used the Karnofsky Performance Scale and found that functional abilities improved from being severely impaired before HAART initiation to within normal limits. Their functional abilities returned to normal at the end of six months of taking HAART. Participants were able to return to or find work and perform everyday activities of daily living with independence.

Many people living with HIV and AIDS find it challenging to attend to daily tasks of living, participate in moderate to physical activities, or have sufficient energy or vitality to engage in an active social life while managing HIV and AIDS (Vosvick et al., 2003). Fatigue is a common symptom in patients with HIV and AIDS; in fact several recent descriptive studies have identified fatigue prevalence rates of 60% (Paddison, Fricchione, Gandhi & Freudenreich, 2009; Voss, 2005). Fatigue or low energy has been associated with a CD4 cell

count of less than 500. This can lead to physical limitations and disability (Ferrando et al., 1998).

Among HIV-positive patients, disease progression is related to decreased energy and increased difficulties with daily activities and pain (Sarna, van Servellen, Padilla & Brecht, 1999). Energy levels and pain can serve as internal distracters that can prevent individuals living with HIV and AIDS from attending to activities of daily living (Myezwa, Stewart, Musenge & Nesara, 2009). These observations have been supported by a study conducted by Lopez et al. (1998) where 72 HIV-infected adults where studied of whom half were taking HAART. According to the study, the majority of the patients reported difficulty engaging in physical activity such as performing household tasks, climbing steps, and carrying out any recreational activities. They attributed their participants' physical difficulties to psychomotor slowing which could be indicative of fatigue.

Makoae et al. (2005) conducted a study on HIV-infected individuals from Botswana, Lesotho and South Africa to describe the presence or absence of personal factors related to HIV and AIDS symptoms. In all, 743 HIV-infected participants from the different countries were recruited to participate. In terms of percentages, the following symptoms which were relevant to the context of this study were cited: Fatigue (56%), fear/worries (44%), headaches (42%), depression (40%), memory loss (27%), anxiety (27%), insomnia (23%), and blurred vision (20%). Interestingly, there were no questions regarding hearing. Hearing and auditory processing play a critical role with regards to interpersonal relationships and the ability to conduct every day affairs especially if they involve communication. Makoae et al. (2005) study was cross-sectional in nature, and the researchers did not comment on whether the participants were taking HAART and no information was collected in terms of how these symptoms impacted on psychosocial activities.

2.7.5 Risk factors for developing HIV – associated neurocognitive disorders.

So what predisposes a person to develop neurocognitive deficits, since incidence and prevalence numbers indicate that not everyone diagnosed as HIV-positive develops HIV-associated neurocognitive disorders? Prior to the HAART era, age, a diagnosis of AIDS, injection drug abuse and the presence of HIV RNA in the cerebral spinal fluid were all indicators of HIV-associated neurocognitive disorders (Grant et al., 2005). Since the advent of HAART, more risk factors have emerged which include gender, education, HAART adherence, CD4 counts, apathy, substance abuse and anaemia.

Age has been found to significantly correlate with HIV-associated neurocognitive disorders (Valcour et al., 2004; Wong et al., 2007; Singh et al., 2010; Ciccarelli et al., 2011). Valcour et al. (2004) found that mild cognitive disorders were identified in 44.7% of older and in 26.3% of the younger participants. HIV-associated dementia was identified in 8.7% of the older participants and only in 3.2% of the younger participants when contributing factors such as sensory or motor findings, depressive symptoms or situational stressors and/or substance abuse were controlled for. Moreover, Singh et al. (2010) reported that age significantly correlated with attention and executive function. Ciccarelli et al. (2011) observed that higher educational levels were associated with reduced risk of neurocognitive impairments and participants older than or equal to 65 years performed significantly poorer on tests that explored attention and executive function, supporting the assertion that aging may result in HIV-associated neurocognitive disorders.

Contrary to these findings, studies conducted in both the developed and developing countries by Berguis, Uldall and Lalonde (1998), Cohen et al. (2001), Jevtovic et al. (2008), Njamnshi et al. (2009) and Sacktor, Wong, Nakasujja et al. (2005), have reported no significant association between age and HIV-associated neurocognitive disorders (HAND).

These studies revealed that younger age was not associated with neurocognitive deficits, or older age with dementia. A shortcoming of the studies conducted by Berguis et al. (1998) and Njamnshi et al. (2009) is that they used screening tests as opposed to full neuropsychological batteries. Nevertheless, this does not diminish the importance of their findings because findings on screening tests have significantly correlated with full battery tests (Struss et al., 1996).

Gender has in some cases been identified as a predictor. It has been asserted that men and women respond differently to neurocognitive assessments (Njamnshi et al., 2009; Singh et al., 2010). Njamnshi et al. (2009) in their Cameroonian study using 185 HIV-infected participants reported that that gender was significantly associated with HAND. Singh et al. (2010) carried out a study in South Africa to establish population normative scores for a select number of neuropsychological tests that could be used in South Africa; they too found that gender correlated with attention and executive function. However, Singh et al. (2010) used a limited number of tests. Furthermore, both studies had more female than male participants and this could have affected their findings.

Regarding education, Ciccarelli et al. (2011) observed that higher education levels were associated with reduced risk of HIV-associated neurocognitive disorders. This was not observed in studies conducted by Cohen et al. (2001), Sacktor, Wong, Nakasujja et al. (2005), and Singh et al. (2010). Cohen et al. (2001) stated that education did not impact performance on neurocognitive tests. Similarly, Sacktor, Wong, Nakasujja et al. (2005) and Singh et al. (2010) also reported that education did not significantly correlate with reduced risk of HAND despite the participants having a mean education of ten years - lower than that reported by Cohen et al. (2001).

The progression of the disease has been shown to greatly impact HIV-associated neurocognitive disorders (HAND). Evidence to support this claim has been provided by Cohen et al. (2004), Valcour et al. (2004), Wong et al. (2007) and Njamnshi et al. (2009) who have stated that low CD4 counts or high viral loads can influence neurocognitive performance. Njamnshi et al. (2009) revealed that HIV-associated neurocognitive disorders (HAND) occurred at all stages of HIV infection but the risk increased with advanced infection. Furthermore the risk of HIV-associated neurocognitive disorders was four times higher in patients with CD4 counts of 200 cells/mm^3 or below. This implies that patients who complain of fatigue need to be screened for anaemia since haemoglobin may serve as an independent risk factor for the development of HAND.

In line with CD4 counts influencing neurocognitive performance, Solomon and Halkitis (2008) and Ettenhofer et al. (2010) maintained that medication adherence significantly correlated with neurocognitive functioning, especially executive functions. Solomon and Halkitis (2008) found that executive function (as measured by the Trail Trials Making Test) significantly correlated with medication adherence. The Trail Making Test assesses the executive function skills of planning, judgement, impulse control and decision, a deficit in any of these areas has potentially life- threatening consequences for individuals living with HIV. Such as not adhering medication regimes, and increasing their risk of HIV re-infection and other sexually transmitted diseases. According to Ettenhofer, Foley, Castellon, and Hinkin (2010), higher levels of medication adherence were predictive of improved functioning in attention, information processing, executive function and motor function. Surprisingly, improved HAART adherence was not prospectively predictive of better learning/memory in their study.

In contrast to the mentioned studies, Sacktor et al. (2005) and Jevtovic et al. (2008) did not find CD4 counts to significantly correlate with HIV-associated neurocognitive disorders. The findings of Jevtovic et al. (2008) showed that there were undetectable levels of HIV RNA in the plasma in 81% of their 96 HIV-positive participants. The undetectable level of HIV RNA did not prevent the presence of mild cognitive motor deficits or HIV-associated dementia. They found that undetectable viral loads did not correlate with fewer neurocognitive problems. Jevtovic et al. (2008) have suggested that optimal HAART efficiency elsewhere in the body does not necessarily translate to viral suppression in the CNS.

A critical appraisal of studies investigating neuropsychological testing and associated risk factors has found mixed findings across all the variables under investigation in this study - age, gender, education and CD4 count. This could due to a number of aspects such as sample size, neuropsychological tests used, race and educational levels, date of onset and whether the participants were on HAART at the time of testing. These reasons do not minimize the importance of investigating the influence of risk factors on how patients with HIV and AIDS perform on neuropsychological functioning because their interaction can either have positive or negative effects on neurocognitive or cognitive-linguistic skills.

In summarizing this section, neuropsychological testing in under resourced developing countries is just an important a tool as neuroimaging techniques in determining the neurocognitive deficits of individuals with HIV and AIDS. Since cortical and subcortical degeneration has been established in the HIV and AIDS population, it is important that the appropriate assessment tools be utilized effectively to detect the presence of neurocognitive deficits or cognitive-linguistic impairments. However, despite their usefulness, neuropsychological tests focus on impairment which is only one aspect of disability

according to the International Classification of Functioning, Disability and Health (ICF). As previously mentioned the current ICF framework was developed from the biopsychosocial approach for health and disability. The biopsychosocial model has been shown to be conceptually, a comprehensive and clinical model that can be applied to HIV-associated neurocognitive disorders especially in the context of this research as depicted in Table 2.9. The biopsychosocial model was introduced as the conceptual model that undergirds this study. For a detailed description on this model and its' factors refer to the conceptual model section 2.3.2.

Table 2.9 The Relationship between the Biopsychosocial Model and the ICF; and the CLQT and Structured Interview Schedule.

BIOPSYCHOSOCIAL MODEL		ICF
Social	Culture Contextual background ARV rollouts Management of ARVs	**Environmental factors** Barriers to access **Participation restriction**
Psychological	Cognitive abilities: - Attention, Memory, Language, Visual Spatial, Executive functions -Neuropsychological methods of assessment Coping strategies Emotions Relationship between language and cognition Risk factors for HAND – education, gender, CD4 count	**Activity** Activities of daily living **Participation** **Personal factors** Internal distractors Social interactions ***Assessment: Structured Interview schedule***
Biological	Neurophysiology: -Cortical and subcortical functioning -Biomedical methods of assessment, Tissue and organ damage: -HIV infection – CD4 count, stages -CNS involment -ARV effects	**Body structure and function** **Impairments** HIV-associated neurocognitive disorders (HAND) ***Assessment: CLQT***

Since the assessment of HIV-associated neurocognitive disorders has been discussed in depth, a description will now be given of how HIV-associated neurocognitive disorders are

treated. An appraisal of how effective antiretrovirals have been in treating HIV-associated neurocognitive disorders will also be given

.

2.8 Treatment of HIV-associated Neurocognitive Deficits or Cognitive- linguistic Deficits

2.8.1 Introduction

The treatment of HIV-associated neurocognitive disorders or cognitive-linguistic deficits can be divided into pharmacological or non-pharmacological treatment. Pharmacological intervention includes antiretrovirals and so-called "adjunctive" therapies that include neuroprotective and neuroregenerative agents. Non-pharmacological interventions can include psychotherapy, mind-body-spirit healing methods, cognitive behavioural therapy, aroma therapy, massage and therapeutic touch, and/or stress management techniques (Kopinsky et al., 2004; Ungrvarski & Trzcianowska, 2000).

Adjunctive therapies and non-pharmacological interventions are beyond the scope of this study and hence will not be discussed. Antiretroviral therapy was introduced and discussed in great depth in section 2.3.4: "Management of HIV and AIDS". The focus of that section was to name the different classes of antiretrovirals and describe how they acted in the body to suppress viral replication, to list the HAART regimens available in South Africa and give a contextual background of how HAART was started in South Africa and current government initiatives pertaining to HAART roll-out in the country and access to all who are HIV-infected. This section will specifically focus on how HAART impacts or treats cognitive-linguistic deficits.

Antiretroviral therapy (ARV) has greatly increased life expectancy for many of those infected with HIV, but as patients survive longer, there is increasing concern that chronic viral neurotoxicity can lead to progressive brain atrophy and associated neurocognitive impairments in some patients. This concern is a valid one because the blood brain barrier (BBB) can prevent permeation of antiviral drugs (Xia et al., 2011). As mentioned above, once the HI virus enters the brain it invades the immune fighting cells such as the macrophages and microglia, causing inflammation, neuronal and dendritic damage which leads to HIV-associated neurocognitive disorders. ARV classes of drugs and individual drugs within classes have different penetration potentials that are dependent upon a variety of biological and virological factors. Unfortunately, only limited data about the penetration of the most widely used antiretroviral agents is available from studies in humans and animals.

Letendre et al. (2006), as cited in Price and Spudich (2008), have rated antiretrovirals on the basis of their CNS penetration effectiveness. They have rated them as 0 (low penetration), 0.5 (intermediate penetration), or 1 (high penetration). According to Letendre et al. (2006), staduvine (d4t), lamiduvine (3TC) and efavirenz (EFV) have a 0.5 penetration. Zidovudine (AZT), neveripine and lopinavir have a rating of 1.0. Unfortunately, even though efavirenz exhibits an average CNS penetration, it also can result in serious neurotoxic side effects as well. Cysique, Maruff and Brew (2004) found a difference in performance between HIV-positive individuals on high CNS penetration HAART and those on low CNS penetration. Those who were on high penetration CNS HAART performed better. However, it is encouraging to note that the antiviral drugs included in the HAART regimens prescribed to individuals living with HIV and AIDS in South Africa have relatively good CNS penetration effectiveness. Therefore it was hypothesized that the cognitive-linguistic abilities of individuals infected with HIV and AIDS in this study would improve on HAART based

upon the relatively good CNS penetration of the antivirals used in HAART on the South African population seeking care at urban government hospitals.

Nucleoside reverse transcriptase inhibitors (NRTI) act to mimic the normal building blocks of HIV DNA and interfere with reverse transcriptase's ability to convert viral RNA to viral DNA. Early studies carried out on zidovudine (AZT) found that individuals performed better on neuropsychological tests once they were given AZT. Zidovudine administered at higher than recommended dosages has been the most successful drug to treat neurocognitive disorders (Ungvarski & Trzcianowska, 2000). AZT is able to cross the BBB by passive diffusion, but the effects are not long lasting (Baldeweg, Catalan & Gazzard, 1998; Kaul & Lipton, 2006; 2007). Later studies have revealed that among NRTIs, AZT (20%) and staduvine (30%) reach brain tissue at concentrations considerably higher than those of didanosine (<4%) (Letendre et al., 2007).

Gibbs, Raschid and Thomas (2003) investigated the movement of lamivudine (3TC) across the guinea pig brain barrier. They found high levels of lamivudine accumulation in the choroid plexus of the guinea pig brain. They believe that the choroid plexus could be a possible entry point for HIV from blood to CSF and could be regarded as a potential reservoir. However, despite the significant accumulation of lamivudine in the choroid plexus there was less lamivudine observed in the cerebral spinal fluid. They detected lamivudine in the brain, but at very low levels, indicating that lamivudine is not easily transported through the BBB. They postulated that this could be due to the fact that lamivudine along with other NRTI bonds with human proteins that prevent it from being transported across the BBB. They have therefore suggested that drug treatment should focus on tackling HIV within the CNS, particularly the choroid plexus.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) serve to inhibit the enzyme reverse transcriptase which is responsible for the early stages of replication by transforming viral ribonucleic acid into viral DNA. NNRTIs are generally, as a class, more strongly protein-bound than NRTIs, which may limit their CNS access. A unique issue with efavirenz is the very common neurological complaints that have occurred when treatment is initiated. More than 50% of treated patients experienced sleep changes (vivid dreams, insomnia, etc.) (Cholewińska & Szymańska 2009). Neverapine is an attractive antiretroviral drug because of its high CNS penetration, which has been documented in trials. Despite having a great molecular weight, it exhibits approximately ten times the BBB penetration than other NNRTIs (Von Giesen, Koller, Thelsen & Arendt, 2002).The NNRTIs such as neveripine and efavirenz have also been shown to improve dementia (Jevtovic et al., 2008).

On the other hand, the findings have been mixed regarding the effectiveness of efavirenz in improving neurocognitive functioning. For example, Jevtovic et al. (2008) have claimed that efavirenz has a positive effect on HIV-associated dementia, and Ciccarelli et al. (2011) have cited efavirenz as having a negative effect on HIV-associated neurocognitive disorders in asymptomatic HIV-infected individuals due to the neurotoxic effects of efavirenz. Despite Ciccarelli et al.'s findings (2011) there is acknowledgement that efavirenz has a relatively good CNS penetration and therefore can be used to manage HIV-associated neurocognitive disorders as long the potential neurotoxicity of the drug is monitored.

Regarding the use of protease inhibitors (PI), Jevtovic et al. (2008), using 96 HIV patients, found that protease inhibitors (PIs) did not readily penetrate the BBB. This was due to their large molecular weight and their propensity to extensively bind to plasma proteins, leaving very little unbound drug to penetrate into the brain and cerebral spinal fluid (CSF). Lopinavir is an excellent example of such a drug. Conversely, Letendre et al. (2007) found

that when Lopinavir was combined with Ritonavir, it was able to reduce HIV RNA found in the cerebral spinal fluid and improve neurocognitive performance. They collected CSF and plasma samples from 14 participants at baseline and 11 again three weeks after taking Lopinavir plus Ritonavir to determine levels of HIV RNA. They also conducted neuropsychological testing on the 14 participants. They found five out of the 14 participants exhibited impaired global performance at baseline. Two of the five impaired participants "dropped out" of the study mid-way. When they retested the remaining three at 12 weeks they found that the participants' neurocognitive performance had improved, reaching normal range. These findings are in contradiction to the findings of Jevtovic et al. (2008) who found that PI-based regimens were not able to prevent the progression of HIV-associated neurocognitive disorders to HIV-associated dementia. Nevertheless, Letendre et al. (2007) contends that the prevalence of HIV-associated disorders after taking HAART could be due to drug resistance, poor adherence, and the level of CNS penetration of some antiretroviral drugs.

Due to antiretrovirals having different CNS penetration it has been suggested that to facilitate effective CNS penetration and improve neurocognitive abilities, a combination of different antiretroviral drugs (HAART) should be given to individuals living with HIV and AIDS rather than providing them with monotherapy.

Given that the incidence of HIV-associated dementia (HAD) has reduced since the advent of HAART, the assumption can be made that HAART must have a definite neuroprotective effect (Bacellar et al., 1994). The mechanisms of chemotherapeutic protection against the development of CNS disease and neurocognitive impairments appear to be related to the suppression of HIV replication as evidenced by a decrease in the viral load and concomitant increase in immune function once therapy is initiated (Kipnis et al., 2008;

Ungvarski & Trzcianowska, 2000). These assertions are supported by the findings of Garvey et al. (2011) who conducted a retrospective study using 251 participants assessing the relationship between CNS disease and CNS penetration effectiveness of different antiretrovirals. They found that CNS diseases occurred more frequently in individuals whose HAART regimen had low CNS penetration effectiveness, than those individuals who were on HAART regimes with higher CNS penetration; yet, this difference was not significant. Although the study was not prospective in nature and only investigated CNS disease and not neurocognitive disorders, it highlights the relationship between CNS disease and CNS penetration effectiveness of different antiretrovirals.

Another study that demonstrated how HAART could improve HIV-associated neurocognitive functioning even if the presence of milder forms of HIV-associated neurocognitive impairments persisted was conducted by Heaton et al. (2010). Part of their study set out to determine the frequency of HIV-associated neurocognitive disorders present in a 1 555 cohort of HIV-positive individuals taking HAART. They found that although HAART had a major impact on CNS manifestations including HIV-associated neurocognitive disorders (HAND), 44% of their participants continued to exhibit milder forms of HAND. They concluded that their patients improved while on HAART because of immune recovery and viral suppression – both systemically (outside the CNS) and in the CNS. Though their study comprised a cross-sectional analysis, it did highlight the persistence of HAND in the era of HAART.

The findings of Heaton et al. (2010) which found that milder forms of HIV-associated neurocognitive disorders still persisted after months of HAART initiation may be explained by a study conducted by Cardenas et al. (2009). They conducted a longitudinal study to investigate the effects of HIV on the brain volume of HIV-positive patients compared to

seronegative controls before and 24 months after HAART. The results revealed that despite being on HAART, individuals living with HIV continued to display on-going brain volume decreases. They purported that this reflected continued viral infection in the brain despite effective viral suppression in the periphery. Because of the limited permeability of blood brain barrier (BBB) to many HAART, they hypothesized that the brain could serve as a reservoir for inactive infected macrophages. So on-going brain injury might have arisen from continued neuronal damage secondary to activated macrophages, in the absence of the virus that might have begun prior to taking ARVs.

In a further longitudinal study with 96 women, Cohen et al. (2001) investigated whether HAART provides functional neurocognitive benefits. They established that neurocognitive performance was much improved by taking HAART for more than 18 months rather than for 12 months or less compared to baseline. Therefore, treatment duration appeared to affect neurocognitive outcome positively, which is worth mentioning given clinical concerns regarding persistence of cognitive impairments. However, according to Cohen et al. (2001), improvement in cognitive performance could have been due to improved overall health status resulting in less fatigue and fewer physical symptoms that might have interfered with performance. Moreover, the general sense of well-being may have been caused by the suppression of viral load and improvement in immune system (Melrose et al., 2008). This may suggest that HAART has a lesser impact on HIV-associated neurocognitive disorders than on other AIDS-defining illnesses, possibly due to the poor CNS penetration of the many antiretroviral agents (Jevtovic et al., 2008).

Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al. (2009) conducted a longitudinal study in Uganda evaluating the effects of HAART, especially staduvine, on HIV-associated neurocognitive disorders. They recruited 102 HIV-positive individuals who

commenced HAART and 26-HIV negative individuals. Their participants comprised of mainly women, with a mean education of 9.6 years and a mean CD4 count of 129. The participants were asked to fill out a functional performance scale (Karnofsky Performance Scale) and underwent neuropsychological testing at baseline, three months and six months. Results revealed that there were improvements across all cognitive domains with significant improvements being noted in executive functions.

However, peripheral neurotoxicity was observed in 30 participants. They presumed this was because of the staduvine-based HAART. Their study was very similar to the current study in that it was a longitudinal study, and they recruited participants with similar demographic characteristic in terms of the sample gender mix, education and CD4 counts. The main difference is that the current study utilized a measure that could ask specific questions about how neurocognition in terms of how cognitive-linguistic abilities impacted upon activities of daily living. Another difference is the strain of HIV-1 under investigation and the functional performance scale. In Uganda the HIV sub-type is A and D (Sacktor, Nakasujja, Skolasky, Robertson, Wong et al., 2006). In South Africa it is sub-type C (Williams & Martin, 2010).

Cook-Easterwood et al. (2007) conducted a study using SCID mice infected with the HI virus to determine whether HAART had any effect on cognitive deficits caused by the HI virus. A SCID mouse is a strain of mice lacking in T and B lymphocytes and immunoglobulins, either from inbreeding with an autosomal-recessive trait or from genetic engineering, used as a model for studies of the immune system (Mosby, 2009). Their results revealed HAART reduced astrogliosis (i.e. the presence of reactive astrocytes that excrete cytokines) and reduced the percentage of HIV-infected cells of SCID mice. However, even though HAART reduced the presence of cytokines that cause neuronal damage, they did not completely

eliminate their presence. Overall, the results of their study suggest that neuronal dysfunction in infected SCID mice, as indicated by dendritic damage and impaired cognition is important in the early pathogenesis and may translate to the human condition. They inferred that early cognitive dysfunction in HAD is related to neuronal damage rather than neuronal death due to the presence of Map-2 which serves as a metabolic marker for dendritic simplification or damage. They also observed that certain viral proteins, such as tat, gp 120 and gp 41, even at low levels, are neurotoxic and might play a role in HIV-associated dementia pathogenesis which has also been suggested by Nath (2002).

While the latter findings are encouraging, more studies designed to address treatment duration and the impact of HAART on neurocognitive functioning are still needed. In fact future research might require a focus on both HAART and so-called "adjunctive" therapies that include neuroprotective and neuroregenerative agents. For example, gene therapy to reverse existing brain injury has been tried and shown to be effective in retarding the progression of Alzheimer's disease (Ellis et al., 2007). Other measures have involved the administration of pharmacological agents. For instance lithium has been shown to prevent the induction of dendritic spine loss and reduce the neurodegeneration caused by HIV-1 gp 120 and thus improve neurocognitive functioning (Letendre, Woods, Ellis et al., 2006). Minocycline which is an antibiotic has been shown to reduce the activation of infected macrophages and microglia in rhesus monkeys, reducing the severity of encephalitis, suppressing viral load and dampening CNS inflammatory markers (Zink et al., 2005). Plans are underway to conduct trials in humans (Ellis et al., 2007). Furthermore, supplementation with vitamins E, B_6, and B_{12} has been shown to improve neurocognitive function. Deficiencies in these vitamins can result in degenerative CNS and PNS disease that interfere with neurotransmission that can cause cognitive and motor impairments.

In summary, HAART has been shown to be the most effective means for improving the cognitive-linguistic abilities of adults living with HIV and AIDS. While significant progress has been made in treating people with HIV-related neurocognitive impairments, these are still occurring in the era of HAART. Considering the potential durability and efficacy of antiretroviral therapies, as well as their variable ability to enter the brain, new questions are being raised about the causes and treatment of HIV-related brain disorders and about the extent to which neuronal dysfunction is reversible. Due to these questions being raised about the treatment of HIV-associated neurocognitive disorders, it is imperative that continual neuropsychological assessment be done to monitor the severity of HIV-associated neurocognitive deficits.

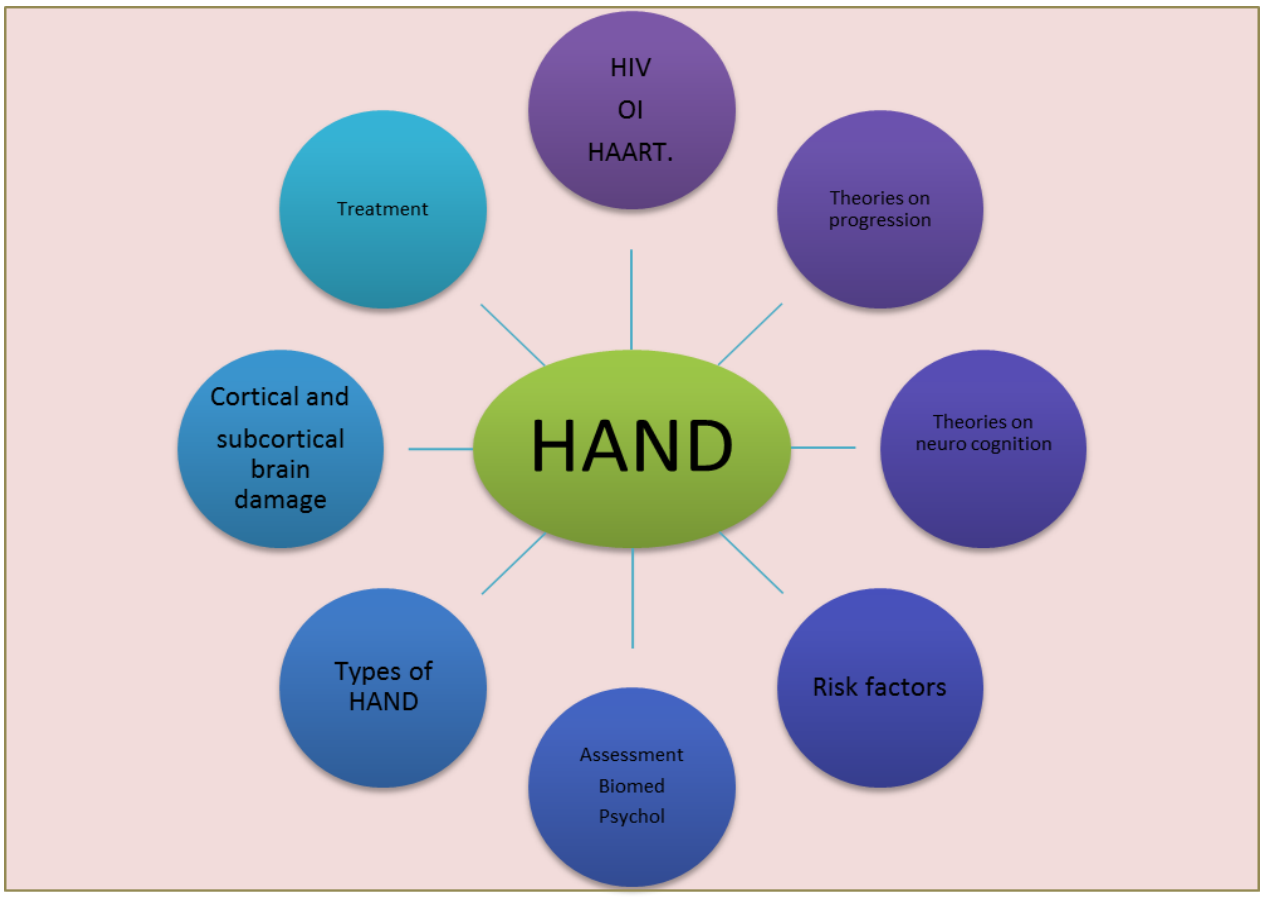


Figure 2.3 Summary of Current Relationships and Linkages Associated to HAND.

2.9 Rationale and Questions

HIV and AIDS as a disease is here to stay unless a cure can be found to destroy it. At present the only effective treatment for HIV and AIDS is HAART. However, despite the era of HAART, the spread of HIV and AIDS continues unabated in Africa, especially in sub-Saharan Africa, with South Africa having the highest prevalence rates. This is due to a number of factors which include the ravages of apartheid, poverty which has resulted in the migration of people seeking work, gender power imbalances particularly in negotiating safe sex practices and the political will of the government in terms of making antiretroviral therapy available to all who have been infected with the HI virus. So it is within this climate of HIV and AIDS that this study is situated.

It is well known that HIV and AIDS wreaks havoc in the body in many ways. The virus is able to cross the blood brain barrier and cause HIV-associated neurocognitive or cognitive-linguistic deficits. These HIV-associated neurocognitive disorders can range in severity from mild to HIV-associated dementia which is the most severe form. HIV-associated cognitive linguistic deficits are hypothesized to be mediated by cortical-subcortical neuronal loops (Woods et al, 2004), which originate in the cortex, extend in the basal ganglia through the thalamus and terminate in the cortex (Murdoch & Whelan, 2009). The severity of HIV-associated neurocognitive deficits is dependent on a number of variables that include the degree of brain degeneration, gender, age, and education and CD4 counts as discussed in this study.

HIV-associated neurocognitive or cognitive-linguistic deficits can be assessed using imaging techniques such as functional magnetic resonance imaging (fMRI) or neuropsychological tests. In the context of South Africa, which is a developing country, the most cost-effective and time-efficient method of assessment is through neuropsychological

assessment. Neuropsychological assessment is able to reveal the cognitive-linguistic skills (attention, memory, language, executive function and visual spatial skills) that might be impaired. As has been highlighted earlier it is thus essential that neurocognitive deficits be assessed and monitored.

Cognitive-linguistic deficits have been identified as a factor influencing levels in medication adherence. Hinkin et al. (2004) found that individuals classified as neurocognitively impaired were 2.5 times more likely to demonstrate poor medication adherence. Additionally, the cognitive domains which have been consistently associated with adherence include attention, executive functioning, attention/working memory, and verbal memory attention, and memory (Hinkin et al., 2004).

Memory deficits have also been indicated as an early sign of brain degeneration if detected early (Panegyres, 2004). Antiretrovirals are important in decreasing the virus and diminishing its effects in the body, so medication adherence is important for general well-being. Treatment interruptions and inconsistent drug intake can lead to inadequate virologic suppression or immunologic response development and spread of resistant viral strains and clinical disease progression (Ammassari et al., 2004). In fact Wilkie (1998) goes as far as to say that minor HIV-associated neurocognitive impairments can predict the risk of mortality.

In addition, HIV-associated neurocognitive disorders, in particular HIV-associated dementia, can have a major impact on public health, both as a result of high levels of assistance required in individual disability, and as a result of the greater health care resource utilization it evokes (Storace et al., 1998). HIV and AIDS as a disease is already having a significant impact on healthcare services and by detecting neurocognitive deficits early on, the burden of disease in South Africa of HIV and AIDS could be alleviated.

Furthermore, in resource-poor environments such as South Africa there tends to be a shortage of trained health personnel. It is usually the neurologist or psychiatrist who diagnoses mild cognitive motor disorders and HIV-associated dementia, and they are not always on hand to diagnose HIV-infected individuals who might exhibit neurocognitive disorders. Therefore the versatility of neuropsychological tests in detecting cognitive-linguistic deficits in developing countries such as South Africa cannot be understated. Neuropsychological tests can be administered by other allied health professionals such as speech language pathologists, neuropsychologists, cognitive psychologists and occupational therapists. Screenings such as the Mini Mental State Exam can be administered by nurses. Assessment by other professionals allows for HIV-infected individuals to receive appropriate clinical management in terms of appropriate referrals and treatment.

By using the Cognitive-Linguistic Quick Test, a test that can be administered by speech language pathologists, the crucial role of speech language pathologists (SLPs) can be highlighted along with their importance in the multidisciplinary management of patients living with HIV and AIDS. SLPs are health professionals trained in the assessment and intervention of cognitive and linguistic disorders. It is important that SLPS not only focus on the individual's expressive and receptive language abilities. The clinician must also assist the individual to cope successfully with neurocognitive deficits as well since cognition and language are intertwined processes (Helm-Estabrooks, 2001; Murdoch & Whelan, 2009).

Since HIV and AIDS cannot yet be cured but can be treated, it classifies as a disability because of its chronic nature. Moreover, due to the fact that HIV-associated neurocognitive disorders are still prevalent in the era of HAART, they can affect an individual's quality of life in terms of being able to perform everyday activities of daily living. This reality falls within the framework of the International Classification of

Functioning, Disability and Health (ICF) which states that disability must be viewed not only in terms of impairment but also include activities and participation of the individual in their immediate environment (WHO, 2002).

According to Webb and Norton (2004), it is important to assess quality of life for several reasons. Firstly, to monitor medication adherence because if a patient is not able to perform activities of daily living it could be due to an inability to follow the complicated drug regimen. In addition, tolerance to HAART – the patient may be experiencing terrible side effects that affect their ability to perform activities of daily living. Furthermore, assessing quality of life via activities of daily living identifies health changes over time and improves communication between patient and health provider.

Bearing in mind the rationale for this research, the researcher set out to answer the following questions:

Question 1: Is there a difference in the cognitive linguistic group performance of adults living with HIV and or AIDS

Question 2: Do the cognitive linguistic abilities of Adults living with HIV/Aids improve after ARV use.

Question 3: Do the variables of age, gender, education, CD4 counts have an influence on the cognitive linguistic abilities of Adults living with HIV and or AIDS.

Question 4: What cognitive – linguistic abilities affect the activities of daily living of adults living with HIV and or AIDS?

Taking cognisance of the literature presented in this chapter, this study sort to investigate the cognitive-linguistic abilities of adults living with HIV and AIDS and their ability to perform Activities of Daily Living before and after antiretroviral therapy. Before the main study was conducted, a pilot study of the Cognitive Linguistic Quick Test and the structured interview scale was conducted to determine the reliability of using these measures for the study.

Chapter 3: Pilot Study

3.1 Introduction

This chapter describes the aims and procedures for determining the reliability of the Cognitive Linguistic Quick Test and the structured interview schedule for this study. The Cognitive Linguistic Quick Test is a test that can be administered by speech-language pathologists, psychologists, occupational therapists, nursing personnel, and other professionals experienced in administering cognitive assessment instruments especially to adults. The researcher is a qualified speech-language pathologist and the research assistants were Masters Students in research psychology who had experience in administering psychometric tests.

This test was standardized on American and Spanish adults who presented with an acquired neurological dysfunction such as traumatic brain injury, dementia, right hemisphere damage, cerebral vascular accidents and has not been used with an adult HIV-infected population that may present with neurocognitive deficits.

As mentioned earlier, a structured interview schedule was also used to determine if cognitive linguistic abilities affected the way individuals conducted their everyday activities of daily living. Since the questions for this schedule were adapted from the Cognitive Symptom Checklists (1993), it was deemed important to evaluate whether the terminology or phrasing of the questions asked what they were supposed to.

3.2 Pilot Study Procedures

3.2.1 Aims.

1. To determine whether the Cognitive Linguistic Quick Test (CLQT) was sensitive enough to detect mild cognitive deficits. Since this was not a comprehensive battery of neurological tests, the researcher needed to determine whether the test could identify participants with mild or minor neurocognitive deficits.

2. To determine if the instructions of the CQLT were easy to understand. Since this test was standardized on a different population from the one that was going to be used in this study, the researcher needed to determine whether the phrasing or terminology used in the questions would affect how the individuals comprehended the questions.

3. To determine whether the CQLT was time efficient. Since the participants were recruited from queues at an outpatient HIV and AIDS treatment clinic, the researcher needed to use a test that would not detain the participants for too long so that they would not lose their place in the queue, or cause them not be interested in coming back for further testing.

4. To determine whether the survey was phrased appropriately and "tapped" into what we were asking. This was important to do since this was a schedule that the researcher had developed and adapted from the Cognitive Symptom Checklist produced by Psychological Assessment Resources Inc (1993).

3.2.2 Description of the participants.

A total of 21 participants (and only 16 were analysed) were recruited from an outpatient clinic situated in Gauteng, a province in South Africa that dispenses antiretrovirals (ARVs). A purposive convenience sampling technique was used. To be included in the study the participants had to be HIV-positive (treatment naïve) and deemed ready to start antiretroviral therapy at this particular clinic. Treatment naive meant that the participants had never been prescribed HAART. Participants were excluded if they were below the age of 18, too sick and or not alert enough to participate. Descriptive statistics that include the mean, standard deviation, frequencies and percentages were run to describe the participants (see Table 3.1 and Table 3.2).

Table 3.1 Descriptive Statistics of the Participants' Demographic Characteristics.

Variable	Mean	Std Dev	Minimum	Maximum	n
Age (in years)	37.63	12.91	20	68	16
CD4 (cells/mm^3)	132.53	70.51	17	243	15
Date of Diagnosis (in months)	8.60	15.87	0	60	15
Education (in years)	9.33	3.03	0	11	12

Table 3.2 Frequencies of Participants' Demographic Characteristics

Variable		n	%age
Gender			
	Female	12	75
	Male	4	25
Employment			
	Unemployed	11	79
	Employed	3	21
Education			
	Primary	1	9
	Secondary	11	91

3.2.3 Testing Procedure for Pilot Study.

The nurse in charge suggested that the participants be recruited when they come for initiation of ARVs, i.e. their first visit for ARVs. Participants were approached by the researcher while in line for initiation of drugs, and asked if they would be willing to participate in the study. The purpose of the study was explained to them and any questions that arose were addressed. Once written consent was obtained to participate in the study and review their medical records, testing commenced.

The CLQT and structured interview survey were administered to all participants. Two trained research assistants administered the test and survey. These trained research assistants- two MA in Research Psychology translated the CLQT and Interview questions into the vernacular namely IsiZulu, Sesotho or Setswana. One was well versed in English and IsiZulu and the in English Sesotho and Setswana. The two research assistants then met with two lectures from the department of languages, in the Humanities Faculties to determine if they had accurately translated the two instruments. One of the lectures was an IsiZulu lecturer and the other Sesotho and Setswana. The two lecturers felt that the translations closely approximated the English version of the tests. Testing took place wherever space was available, either in an empty doctor's room or a cordoned-off section of the waiting area where dispensing of the ARVs took place. The researcher and participant sat on opposite ends of the desk and testing commenced. The participants were provided with a pen or pencil to perform the written tasks. The CQLT took approximately 40 to 50 minutes to complete. The survey was conducted face to face and it took approximately 25 minutes to complete. All measures were administered and scored according to standard procedures.

3.2.4. Data analysis.

Descriptive statistics were obtained for demographics and the CLQT. The data on the CLQT was collected and raw scores were obtained and categories of severity (mild, moderate and severe) were determined by looking at what range of severity the raw score fell into. Frequency counts (which were converted to percentages) were used to analyse the data.

3.3 Results

Results were presented according to the aims of the pilot study:

1. *To determine whether the CQLT was sensitive to mild neurocognitive deficits.*

Table 3.3 Severity Rating of the participants Cognitive - Linguistic abilities (N=16).

Cognitive -ling abilities	**normal** n(%)	**mild** n(%)	**moderate** n(%)	**severe** n(%)
Attention	3(19)	11(68)	0	2(13)
Memory	3(19)	5(31)	5(31)	3(19)
Executive Functions	3(19)	5(31)	3(19)	5(31)
Language	8(50)	5(31)	3(19)	0
Visual Spatial	4(25)	10(62)	2(13)	0

Table 3.3 revealed that the majority of participants (68%) exhibited mild attention deficits. In addition, the majority of the participants exhibited mild (31%) or moderate (31%) memory deficits. Results also revealed that 81% of the participants had deficits in executive functions. Surprisingly, only 50% of the participants presented with language deficits that were

mainly in the mild range. Results also revealed that (63%) of the participants exhibited mild visual spatial deficits and 13% fell in the moderate range.

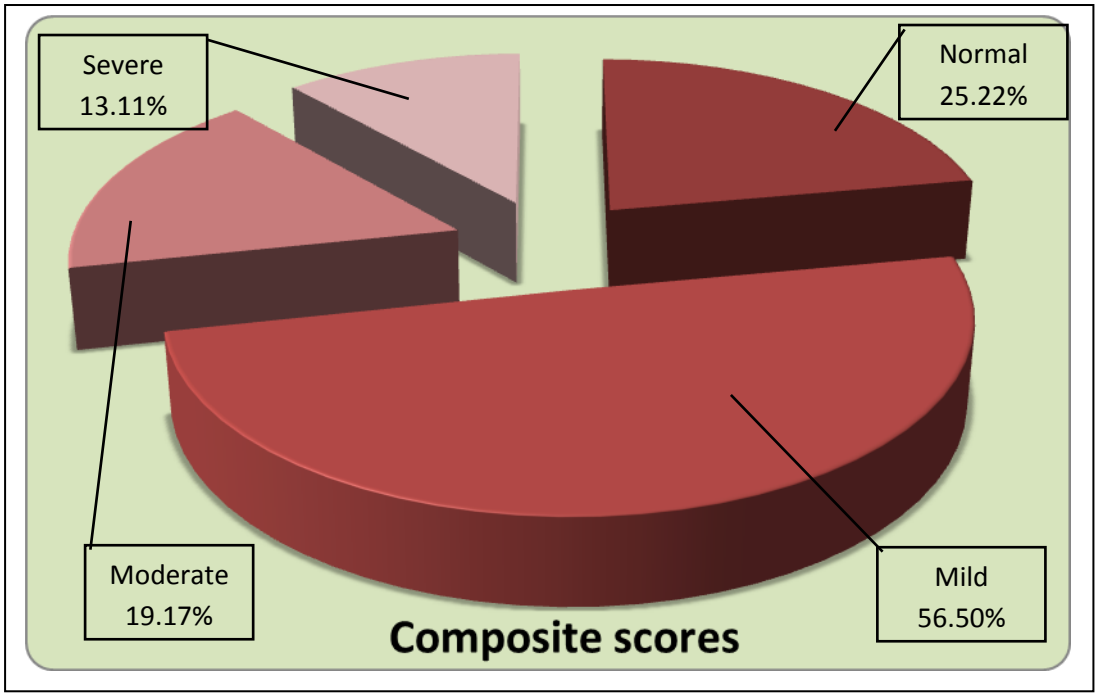


Figure 3.1: Percentage severity rating of participants who exhibited deficits across all cognitive domains

The majority of participants (87.5%) in this study presented with some form of cognitive deficit, and more than half of them (56%) showed mild problems.

From the above results it was determined that the CQLT was a test that was sensitive enough to detect mild cognitive deficits and was therefore suitable to be used in the main study.

2. To determine if the instructions of the CQLT were clear and simple to understand.

This was determined by noting how many patients asked the instructor to repeat the questions. Each participant was allowed a maximum of two repetitions, i.e. before the examiners started noting how repetitions were requested. Participants generally required no more than two repetitions even when presented in the vernacular. Based upon these findings, the CQLT was deemed appropriate to use in the study.

3. *To determine whether the CQLT was time efficient.*

The examiners recorded how long it took to conduct the tests with the patients, and an average time was calculated. On average it took approximately 25-35 minutes to complete the test. This time was found to be reasonable. On further inspection it was noted that some of the questions were redundant and these were removed. After revising the questions, it was found that the survey took approximately 10 -15 minutes to complete. This was found to be a reasonable time in which to complete the survey.

4. *To determine whether the structured survey questions were phrased appropriately and whether the participants understood what was being asked.*

This was determined by noting how many participants asked the instructor to repeat or rephrase the questions. Each participant was allowed a maximum of two repetitions, i.e before the examiners started noting how repetitions were requested. Some participants required more than two repetitions even when presented in the vernacular. Based upon these findings, the questions were simplified and redundancy was eliminated. The survey was deemed appropriate to use in the study because it elicited information on how specific cognitive linguistic domains impacted upon activities of daily living.

3.4 Challenges

The participants arrived very early at the clinic to queue up for their blood test(s) and medications. So by the time we asked them to participate in the study they were tired and sometimes hungry. As a result the researchers experienced difficulty getting the patients to come back and complete the testing once they heard their names called over the public address system. Due to this challenge another location within the clinic was found where participants could be recruited just before they were initiated in the counselling department.

Another challenge was to persuade the doctors and nurses to assist the researchers in terms of allowing the patients to keep their place in the queue if they were pulled out for testing. This was circumvented by approaching the participant at the wellness clinic, before counselling sessions started.

Reliability and consistency of the research assistants presented another possible challenge. After the pilot study, new research assistants were hired. However, since these research assistants were Master's students in the psychology and audiology departments who had just enrolled in the programmes, there was little risk of them leaving before all the data could be collected for the main study.

Of the 21 participants who were recruited for the pilot study only 16 response sheets could be analysed. This was due in part to participants not returning to complete testing and erroneous capturing of data. This was later rectified by recruiting patients before they entered the wellness counselling sessions. Erroneous data capturing was corrected by thoroughly training the research assistants.

3.5 Conclusion

The Cognitive Linguistic Quick Test was deemed appropriate to use in this study even though it had not been used on a South African adult population living with HIV and AIDS. . The

CLQT was able to identify clear deficits in all five cognitive domains, and as reported in the literature using more expensive, elaborate and time-consuming neuropsychometric evaluations (e.g. Berghuis, Uldall & Lalonde, 1999; Savage, Jackson and Sourathathone, 2003). It was found to be time efficient and questions could easily be translated into the vernacular and understood by the clients. In addition it was easy to score and determine severity ratings. This suggested that the CQLT was an appropriate instrument for use in the initial investigation of cognitive deficits in patients with HIV or AIDS in South Africa.

It was also decided that the structured interview schedule would be suitable for eliciting the responses on how cognitive linguistic abilities impact upon activities of daily living after questions were simplified. Once the pilot study was conducted and results determined, the main study was implemented.

Chapter 4: Methodology

4.1 Introduction

In this chapter the methodology for this study is presented. The study design, participant description, measures used and study procedure will be presented since the pilot study indicated that the measures were appropriate to use in this study. Reliability along with threats to reliability will also be discussed.

It should be noted that after the data was collected, the National Department of Health had adjusted its criteria for initiation of HAART in line with the WHO (2010) regulations regarding HAART initiation. They changed them from having a CD4 count of 200cells/mm^3 to 350cell/mm^3.

4.2 Aims

The aims of this study were as follows:

1. To determine whether there is a significant difference in cognitive-linguistic abilities between the experimental, comparison and cross-sectional groups on the Cognitive-Lingusitic Quick Test and the interview schedule.

   Hypothesis: There is a difference in the cognitive - linguistic abilities of the three groups of adults living with HIV and or AIDS

2. To determine whether there is a significant difference in cognitive-linguistic abilities within the participants (time effect) for the experimental and comparison groups on the Cognitive-Lingusitic Quick Test and the interview schedule.

   Hypothesis: The cognitive linguistic abilities of adults living with HIV/Aids improve after HAART use across the three testing times. Or There is a within group difference in cognitive linguistic abilities across the three testing times.

3. To determine the effect of age, gender, education, CD4count on cognitive-linguistic functioning in both the experimental and comparison groups at baseline, four months and eight months on the Cognitive-Linguistic Quick Test and the interview schedule.

   Hypothesis: The four variables have an influence or effect on the cognitive- linguistic abilities of adults living with AIDS before and after HAART use.

4. To describe the cognitive-linguistic abilities that affect performance and activities of daily living in the experimental, cross-sectional and control groups.

   Question: Do cognitive – linguistic abilities affect activities of daily living.

4.3 Research Design

The study incorporated a multiple group time series research design. The research design was quasi-experimental in that the participants recruited for the study were not obtained through true random sampling (Rosnow & Roberts, 2002). Purposive sampling was used in the study because the researcher had to recruit clients who were representative and typical of people with HIV and AIDS in South Africa. Furthermore, purposive sampling was

used due to time restraints and accessibility of participants. The experimental component of the study involved the manipulation of an independent variable (namely ARV use), pre- and post-testing and the use of a comparison and cross-sectional group. The dependant variable was the cognitive and language abilities of the participants. In addition, the time series design was used because the dependant variable was measured repeatedly: before HAART initiation, four months and eight months after HAART initiation. In this way the effects of treatment could be fully investigated. These time frames were chosen because they coincided with the times that the ARVs were dispensed to the participants.

Cognitive and linguistic abilities are subject to the effects of time, and could be evolving as HIV and AIDS progresses; hence it was felt that assessing individuals over time would yield more realistic data on the participants' cognitive and linguistic abilities. The longitudinal nature of the study allowed for each participant to serve as their own control which allowed the researcher to document intra-variable changes in each participant. Since, the participants served as their own "controls", there was no need for matching subjects on extraneous variables in the comparison and cross-sectional groups. In addition, differences in performance could be attributed to the use of ARVs despite differences in individual performance. Furthermore, use of this design allowed for within-subject comparison which is said to offer greater statistical power relative to sample size (Devlin, 2006; Maxwell & Satake, 2006). A comparison group was included in the study to be able to attribute any changes in performance in the experimental and cross-sectional groups regarding cognitive and linguistic abilities to the effects of the ARVs. The comparison group was included to reduce the confounding effects of age, gender and history such as psychosocial and medical diagnoses. A cross sectional group was also included to serve as a comparison reference group to the experimental group.

Even though the research design was primarily quantitative, a qualitative aspect was included. This was done to broaden the scope and depth of information that could be obtained to increase our understanding of how HIV and AIDS affects an individual's cognitive and linguistic functioning. The study was quantitative in nature in that it included the use of a standardized test to assess the cognitive and linguistic abilities of the participants. The qualitative aspect of the study included the use of a structured interview schedule that investigated how the participant's cognitive and linguistic abilities impacted upon their activities of daily living. The structured interview was included to compliment the findings of the Cognitive Linguistic Quick Test and so as to effectively describe the phenomena under investigation – the cognitive linguistic abilities of adults living with HIV and AIDS.

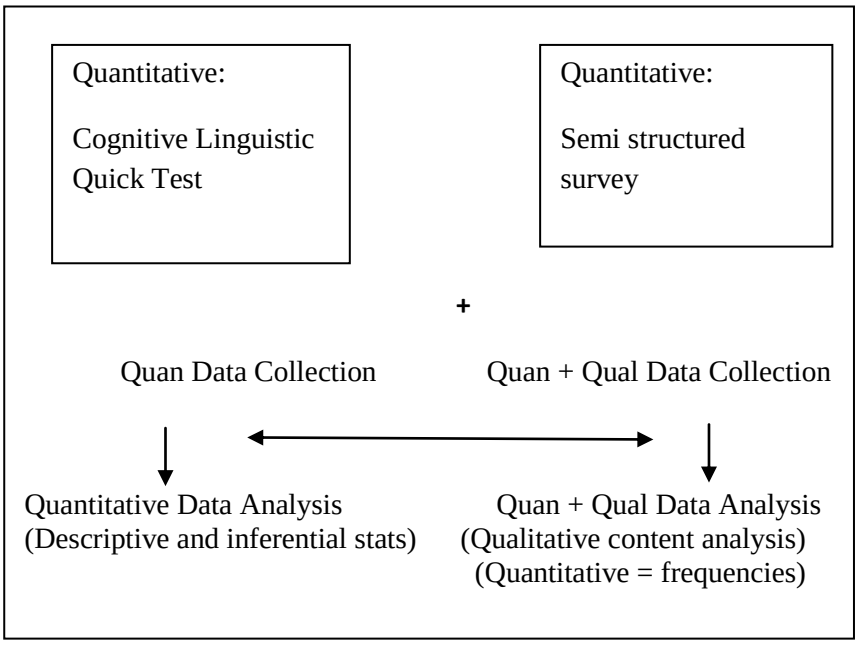


Figure 4.1 Diagram of Research Design

4.4 The Sample

Participants were recruited from an out-patient clinic affiliated with a government hospital in Johannesburg, Gauteng. This hospital is a secondary level government hospital

under the Gauteng Province Department of Health. The hospital is a large, urban public hospital housing one of the largest public sector HIV and AIDS treatment sites in South Africa. The out-patient clinic is a national ARV roll-out site that has been treating HIV and AIDS patients and dispensing ARVs for ten years. The majority of patients are referred to the clinic by the hospital with which it is affiliated. The patients attending the clinic have already been diagnosed with HIV and AIDS and are seen for general HAART or ARV drug intervention. The participants in the study were eligible to receive antiretrovirals from the clinic.

4.4.1 Sampling procedure.

A non-probability purposive sampling procedure was used to recruit potential participants from the out-patient clinic. Non-probability sampling was used because participants were selected on the basis of convenience and method of recruitment (Feild, Pruchno, Bewley, Lemay & Levinsky, 2006). Participants were approached as they were waiting in the clinic vestibule and asked whether they would be interested in participating in the study. These patients needed to be diagnosed as HIV-positive and be eligible for medical management and counselling. Participants were recruited into three groups: experimental (longitudinal), control (comparison) and cross-sectional. Even though the participants were not recruited using random measures, the sample was a representative group of the population of individuals with HIV and AIDS in South Africa accessing treatment from a public health site. They were also representative of the urban HIV population (see section 2.2) in that they were predominantly female, black, in their mid- to late thirties, unemployed, with some secondary education irrespective of gender (Rosen et al., 2008).

Inclusion criteria.

- Adult male and female HIV-positive patients with a CD4 count of < 200 cells/mm3 or higher, but who are symptomatic. According to the South African HIV and AIDS roll-out policy or regulation, patients are only eligible for HAART at a CD4 count of 200 cell/mm3 or higher but who are symptomatic.
- Enrolled to commence HIV treatment (ARVs) at the out-patient clinic.
- Treatment naïve, i.e. have never received HIV and AIDS treatment before.
- Participants were required to be within the age range of 18 – 60 years. The ceiling of 60 years was used in order to minimize the effects of age as a confounding variable. Individuals under 18 were not included in this study due to the different way the virus manifests itself in adults when compared to children (Larson, 1998; Koekkoek, Sonneville, Wolfs, Lichta & Geelen, 2007). Sixty years was the upper limit in age due to the effects of aging on cognition after 70 years.
- Participants needed to be alert, oriented, able to provide informed consent and able to participate in the testing session.
- Fluency in English was not a requirement for inclusion in the study since all evaluations were translated into the main vernacular languages.

Exclusion criteria.

Potential participants were excluded from the study for the following reasons:

- If they exhibited a fever of more than 37.5^{0}C, had an active psychiatric disorder, were alcoholics, suffered a hearing loss and/or suffered from a severe medical illness that would interfere with their ability to participate in the study.
- If they were unable to provide informed consent due to limited levels of alertness.

- If they had or reported a history of a head injury with loss of consciousness for more than 30 minutes.
- If they presented with or reported having cerebrovascular accidents, seizure disorders, past psychiatric history, visual defects, head injury and or pre-morbid learning disability as determined via demographic items.

4.4.2 Demographic description of participants.

Descriptive statistics are presented below to describe the participants recruited in this study.

Experimental group.

At baseline 110 participants were recruited and tested, but only 55 of the 110 were re-tested at 4 months, and 51 participants were re-tested again at eight months. The 55 participants tested at baseline who were not retested formed the baseline participants for the cross sectional group. The experimental group included participants who had undergone the necessary counselling sessions and knew they were eligible for HAART initiation. They were told at baseline testing that they would be followed up at four months and at eight months. These months coincided with their medical check-ups See Table 4.1 and Table 4.2 for a description of the participants.

There was a high attrition of participants from baseline (110) to four months (55). The attrition occurred for a number of reasons. The participants after initial testing died, refused to be tested again, or were too ill to travel. In addition a number of the participants could not be contacted, decided not to take ARVs despite having gone through the counselling, or they had already gone to the clinic and refilled their prescription of ARVs. The population serviced by

this clinic tended to be a very migrant and some of the participants when contacted reported that they had moved away from the area and had decided to visit an HIV and AIDS clinic in the vicinity.

Table 4.1 Frequencies for Gender, Race, Education, Employment and Regimen in the Experimental group

		Baseline		4 months		8 months	
Group	**Variable**	**N**	**n**	**N**	**n**	**N**	**n**
Experimental	Gender	55		55		51	
	Male		18(33%)		18(33%)		17(33%)
	Female		37(67%)		37(67%)		34(67%)
	Race						
	Black		46 (84%)		46 (84%)		45(86%)
	Coloured		9 (16%)		9 (16%)		7(13%)
	Education						
	Primary		7(13%)		7(13%)		6(12%)
	Secondary		43(78%)		43(78%)		39(80%)
	College		5(9%)		5(9%)		4(8%)
	Employment						
	Employed		19(34.5%)		23(42%)		18(35%)
	Unemployed		36(65.5%)		32(58%)		33(65%)
	Regimen						
	1a		0		53(96%)		50(98%)
	1b		0		2(4%)		2(4%)

The frequency statistics presented in Table 4.1 show that there were more male participants, predominantly black, with either some level of formal primary or secondary education and mainly jobless. The majority of the participants were on 1a HAART regimen that included staduvine (NRTI), lamivudine (NRTI) and efavirenz (NNRTI).

Table 4.2 Descriptive statistics for Age, Education and CD4 counts for the Experimental group.

Group	Time	Variables	Mean	Std Dev	Min	Max	N
Experimental	Baseline	Age	37.71	8.62	23	58	55
		Education	9.93	2.52	2	13	55
		CD4	134	55.6	3	359	55
	4 months	Age	38.15	8.58	23	59	55
		Education	9.93	2.52	2	13	55
		CD4	186.36	111.56	10	504	44
	8 months	Age	38.94	8.65	25	60	51
		Education	9.92	2.60	2	13	51
		CD4	190	115.20	20	600	40

Std.Dev= standard deviation
"N" does not necessarily correspond with those reported in the frequency tables because not all participants' files included the information e.g CD4 counts

Descriptive statistics presented in Table 4.2 reveal that the average age of the participants in the experimental group was 37 (SD=8.62) to 39 (SD=8.65) years. The mean years of education for the experimental participants were nine to ten years. At baseline, mean CD4 count was 134 cells/mm^3 (SD=55.6) and at eight months the mean increased to 190 cells/mm^3 (SD=115.2). CD4 counts are not always taken at the time of a medical check-up or if blood samples were drawn participants did not always return to the reception area to report CD4 counts; hence results were only reported at baseline and at eight months.

Comparison group.

These participants were recruited via the same sampling technique. This group included participants who for whatever reason elected not to receive ARV, but attended the clinic for medical monitoring on a regular basis. The comparison group was included in the study to make sure that any changes in the cognitive-linguistic abilities were due to the effects of the

ARVs. Twenty-one participants were recruited and tested at baseline, ten were re-tested at four months and nine were retested again at eight months. See Table 4.3 and Table 4.4 for a description of the participants.

The researcher found it very difficult to recruit for this group hence the unequal sample size of the comparison and experimental group. Most participants despite being diagnosed as HIV positive had relatively high CD4 counts that did not meet the inclusion criteria. As a result there were not many people whom the researcher could recruit. Lastly after initial testing some participants became eligible to initiate ARVs because their CD4 count had dropped. Attrition was also high for the same reasons as the experimental group and those mentioned in the latter.

Table 4.3 Frequencies for Gender, Race, Education, Employment and Regimen in the Comparison group

		Baseline		**4 months**		**8 months**	
Group	**Variable**	**N**	**n**	**N**	**n**	**N**	**n**
Comparison	Gender	21		10		9	
	Male		12(57%)		4(40%)		4(44%)
	Female		9(43%)		6(60%)		5(56%)
	Race						
	Black		21(100%)		10(100%)		9(100%)
	Education						
	Primary		6(28.5%)		2(20%)		2(22%)
	Secondary		12(57%)		6(60%)		5(56%)
	College		2(9.5%)		1(10%)		1(11%)
	University		1(5%)		1(10%)		1(11%)
	Employed						
	Unemployed		8(38%)		2		2(22%)
	Employed		13(62%)		8		7(77%)
	Regimen						
	1a		0		0		0
	1b		0		0		0

The frequency analysis (see Table 4.3) revealed that the majority of the participants were female, black, with some formal primary or secondary education and no formal work.

Table 4.4 Descriptive statistics for Age, Education and CD4 counts for the Comparison group

Group	Time	Variables	Mean	Std Dev	Min	Max	N
Comparison	Baseline	Age	39.48	11.47	24	60	21
		Education	8.38	4.70	0	14	21
		CD4	406.13	185.04	253	600	15
	4 months	Age	37.00	9.19	25	54	10
		Education	8.40	4.87	0	14	10
		CD4					
	8 months	Age	37.56	9.76	25	54	9
		Education	8.78	5.31	0	14	9
		CD4	265.63	137.92	100	430	8

Std.Dev= standard deviation
"N" does not necessarily correspond with those reported in the frequency tables because not all participants' files included the information e.g CD4 counts

Descriptive statistics (see Table 4.4) revealed that the average age of the participants in the comparison group was 37 (SD=9.76) to 39 (SD=11.47) years. The mean years of education for the comparison participants were eight to nine years. At baseline, mean CD4 count was 406 cells/mm^3 (SD= 185.04) and at eight months the mean decreased to 265 cells/mm^3 (SD=137.92). CD4 counts were not always taken at the time of a medical check-up or if blood samples were drawn participants did not always return to the reception area to report CD4 counts; hence results are only reported at baseline and eight months.

Cross sectional group.

A cross sectional comparison group was included in the study for several reasons: The attrition rate in the experimental group was high; to rule out practice effects since the time between testing was under six months; and to establish normative trends that could be compared to the experimental group in terms of the effects of HAART on cognitive-linguistic abilities. The participants were recruited via the same sampling technique. Furthermore, the frequency and descriptive stats presented by the cross sectional groups (refer to Table 4.5 and 4.6) were comparable to those of the experimental group. Patients attending this clinic at the time of testing could only start ARV treatment with CD4 counts of 200cells/mm^3 or below. Therefore the CD4 counts of the participants in the experimental and cross sectional were more or less within the same range at the scheduled medical and prescription refill appointment(s). Due to the aforementioned the cross sectional group was served as a reference comparison group.

Fifty-five out of 110 participants who were recruited at baseline and not followed up at four and eight months were included as this group's baseline. Another 43 participants were recruited at four months and a further 40 participants at eight months. See Table 4.5and Table 4.6 for a description of the participants.

The vertical and horizontal lines in the tables indicate three different, separate groups of participants recruited anew at each of the three testing time.

Table 4.5 Frequencies for Gender, Race, Education, Employment and Regimen in the Cross-sectional group

Group	Variable	Baseline (Group 1) N	Baseline (Group 1) n	4 months (Group 2) N	4 months (Group 2) n	8 months (Group 3) N	8 months (Group 3) n
Cross sectional	Gender	55		43		39	
	Male		26(47%)		10(23%)		7(17.5%)
	Female		29(53%)		33(77%)		33(82.5)
	Race						
	Black		54(98%)		42(98%)		38 (95%)
	Coloured		0		1(2%)		2 (5%)
	White		1 (2%)		0		0
	Education						
	Primary		16(29%)		6(14%)		8(19.5%)
	Secondary		31(56%)		27(63%)		26(65%)
	College		8(15%)		10(23%)		5(12.5)
	Employed						
	Unemployed		22(41%)		10(33%)		5(12.5%)
	Employed		33(49%)		33(67%)		35(87.5%)
	Regimen						
	1a		0		39(91%)		36(90%)
	1b		0		2(4.5%)		1(2.5%)
	2		0		2(4.5%)		3(7.5%)

The frequency statistics (see Table 4.5) showed that there were more male participants, predominantly black, with either some level of formal primary or secondary education, and mainly unemployed in the cross sectional group. The majority of the participants were on 1a HAART regimen that included stavudine (NRTI), lamivudine (NRTI) and efavirenz (NNRTI).

Table 4.6 Descriptive statistics for Age, Education and CD4 for the Cross-sectional group

Group	Time	Variables	mean	Std Dev	Min	Max	N
Cross sectional	Baseline (Group 1)	Age	41.13	8.94	18	60	55
		Education	8.58	3.78	0	14	55
		CD4	125.76	83.51	3	392	38
	4 months (Group 2)	Age	38.21	8.72	25	58	43
		Education	9.93	2.65	3	14	43
		CD4	149.20	105.19	3	570	41
	8 months (Group 3)	Age	38.87	9.66	26	67	39
		Education	10.08	2.27	6	14	38
		CD4	328.74	136.08	49	736	39

Std.Dev= standard deviation
"N" does not necessarily correspond with those reported in the frequency tables because not all participants' files included the information e.g CD4 counts

Descriptive statistics (see Table 4.6) revealed that the average age of the participants in the cross sectional group was 39 to 41 years. The mean years of education for the experimental participants were eight to ten years. At baseline, the mean CD4 count was 125cells/mm^3 and at eight months the mean increased to 328 cells/mm^3.

The frequency and descriptive stats presented by the cross sectional groups were comparable to those of the experimental group. Patients attending this clinic at the time of testing could only start ARV treatment with CD4 counts of 200 cells/mm^3 or below. Therefore the CD4 counts of the participants in the experimental and cross sectional were more or less within the same range at the scheduled medical and prescription refill appointment(s).

4.5 Instruments

Research instruments included the Cognitive Linguistic Quick Test (CLQT) and a structured interview schedule.

4.5.1 The Cognitive Linguistic Quick Test.

The Cognitive Linguistic Quick Test (CLQT) was developed to assess the cognitive and linguistic functions of adults (18-89 years old) with neurological dysfunction (Helm-Estabrooks, 2001) (see Appendix V). The CLQT enables clinicians to quickly assess the five domains of cognitions, namely attention, memory, executive functions, language and visual spatial skills.

- Attention is crucial to a wide array of everyday tasks. Attention is multifaceted behaviour that includes different types of abilities such as vigilance, selection (sustain attention in the presence of distraction) and working memory (temporary storage and manipulation during information processing) (Helm-Estabrooks, 2001).
- Memory is a process that enables us to attend to and register new information, retain, process and store (learn) this information and retrieve it.
- Executive functioning is the ability to plan, sequence, implement and accomplish goal-directed activities in a flexible manner. This skill is critical for the performance of all non-routine and independent tasks (Helm-Estabrooks, 2001).
- Language is a person's ability to express thoughts and ideas and understand what is spoken to them.

- Visual Spatial (perception) is the ability to scan, discriminate, analyse, recognize and interpret what is seen.

The test was composed of ten tasks, which included personal facts, symbol cancellation, confrontational naming, clock drawing, storytelling, symbol trails, generative naming, design memory, mazes and design generation. The test was administered in English, IsiZulu and Sesotho. IsiZulu and Sesotho were chosen because of all the vernacular languages they are the most widely spoken and understood in Gauteng. Personal facts which had four items required the participant to answer questions pertaining to their date of birth, place of birth and address. Maximum and minimum possible scores for the participant to obtain for personal facts were eight and zero respectively. Symbol cancellation required the participants to cross out symbols that did not match the target symbol from four quadrants on the page. Maximum and minimum possible scores for the participant to obtain for symbol cancellation were 12 and zero respectively. Confrontational naming which had ten items entailed naming pictures. Maximum and minimum possible scores for the participant to obtain for confrontational naming were ten and zero respectively. Clock drawing which had 11 elements involved drawing a clock depicting the time participants were given. Maximum and minimum possible scores for the participant to obtain for clock drawing were 13 and zero respectively. Story retelling which was composed of 18 elements required the participants to repeat a short story told to them. Maximum and minimum possible scores for the participant to obtain for story retelling were 18 and zero respectively. Symbol trails which had two trails and one scored item required the participants to draw lines that connected either circles and triangles; alternating circles and trials; and lastly alternating circles and triangles of increasing size. Maximum and minimum possible scores for the participant to obtain for symbol trails were 10 and zero respectively. Generative naming entailed generating as many items belonging to the

category of animal and starting with the letter “m” under 60 seconds. Maximum and minimum possible scores for the participant to obtain for generative naming were nine and zero respectively. Design memory which had three items involved participants matching designs to the target design. Maximum and minimum possible scores for the participant to obtain for design memory were nine and zero respectively. Mazes included drawing lines through two mazes with different levels of difficulty. Maximum and minimum possible scores for the participant to obtain for mazes were eight and zero respectively. Design generation entailed generating different designs using four straight lines. Participants were provided with 13 opportunities to generate designs. Maximum and minimum possible scores for the participant to obtain for design generation were thirteen and zero respectively. For a summary of maximum and minimum scores on these subscales refer to Table 5.8 in the results section.

The validity of the CLQT was determined by test content, relation to other variables and internal structure.

CLQT tasks were designed to tap specific cognitive and language skills. The tasks chosen had been shown by research and proven by clinical practice to tap into cognitive and language skills. Evidence based on test content was determined from the results of the pilot study. “The test was checked for evidence of construct irrelevant components and construct under representation by various experts including the author and others. To the degree that the test did not provide full construct representation or contained elements that were construct irrelevant (including potentially biased items), the test was modified to eliminate such problems.”(Helm-Estabrooks, 2001, p.126) For example, the instruction given to the participants had to be modified to maximize comprehension of some the tasks.

To determine relationship between test scores and variables external to the CLQT provided another important source of validity evidence (Helm-Estabrooks, 2001). Therefore a correlation analysis was performed to determine the relationship between clock drawing severity rating and the composite severity rating of the Cognitive Linguistic Quick Test. The Pearson correlation coefficient was found to be 0.74 (Helm-Estabrooks, 2001). The clock drawing was considered to be a mini screen of cognition (Helm-Estabrooks).

Evidence of internal structure was compiled by performing confirmatory factor analysis. This was done by looking at the difference in performance between non clinical and clinical examinees. "Structural equation modelling was used to conduct confirmatory factor analysis on each of the five domain subscales. One-factor measurement models were constructed for each subscale and fit to the standardisation data. Absolute fit measures used to assess the adequacy of each model fit to data included the likelihood ratio chi-square statistic, the relative chi-square statistic and the Root Mean Square Error of Approximation (RMSEA)." (Helm-Estabrooks, 2001, p.126). Values of less than 3.00 were considered acceptable values of absolute fit of the model to the data. A values of less than 0.08 for the RMSEA and greater than 0.09 for the Non-Normed fit Index (NNFI) were considered appropriate (Helm-Estabrooks, 2001). The expected Cross-Validation Index (ECVI) was also derived. The confirmatory measurement models representing the five cognitive domains are presented in Appendix VI.

To determine whether the CLQT could indicate the presence of a cognitive disorder between clinical and nonclinical individuals- a t-test was conducted. The results of the t-test procedure revealed between the matched clinical and nonclinical examinees for all 10 CLQT tasks and the cognitive domains (Helm-Estabrooks, 2001) refer to Appendix VI.

The reliability of CLQT was determined by means of test-retest correlation, standard error measurement (SEM) and inter-scorer agreement. The stability or test-retest correlation was measured by administering the test one group of examinees on two separate occasions (Helm-Estabrooks, 2001). The test was administered on 46 nonclinical examinees. That is examinees who did not present with any brain involvement. The test –retest means and standard deviations, stability coefficients, standard error measurement and mean absolute score differences are presented in Appendix VI. The test-retest stability coefficients ranged between 0.03 and 0.81 for the tasks. The test-retest stability coefficients ranged between 0.61 and 0.90 for the cognitive domains. The SEM ranged between 0.57 and 1.84 for the tasks. The SEM ranged between 1.16 and 16.57 for the cognitive domains (Helms-Estabrooks, 2001) (refer to Appendix VI).

An absolute score difference was also calculated for this test. "The results showed that the absolute score differences were generally small, (less than one point difference for all tasks, except for Symbol Trails and Design Generation), indicating high consistency of scores across administrations." (Helm-Estabrooks, 2001, p.125).

Regarding the inter-scorer agreement, only eight out of the ten tasks were objectively scored. The other two tasks - clock drawing and Generative Naming which required clinical judgement, were scored using rules that were agreed upon by the two scorers. The overall correlation between two scorers for clock drawing and generative naming was 0.86 and 0 .99 respectively.

4.5.2 Interview schedule.

The semi-structured interview was included to compliment the Cognitive Linguistic Quick Test. The questions used in the interview were generated from existing theory and research. In this case the five recognized domains of cognition (attention, executive functions, visual spatial, language and memory) were identified as the key concepts for initial coding categories. The survey questions were adapted from the Cognitive Symptom Checklist produced by Psychological Assessment Resources Inc. (1993). A structured interview schedule containing mostly closed-ended questions with an open-ended questions (refer to Appendix VII) was used to compliment the findings of the CLQT and explore the impact cognitive linguistic abilities might have on activities of daily living. Open-ended questions allowed the participants to expand, justify and provide their own answers to questions(Maxwell & Shitake, 2006).The responses from the open ended questions provided more interpretation and discussion around activities of daily before and after HAART (Babbie & Mouton, 2001).

Closed-ended questions served as probes to specifically explore how activities of daily living were being conducted under each cognitive domain (Maxwell & Shitake, 2006). Closed-ended questions allowed for more uniformity and were easier to analyse. Interviews were conducted individually. The questions were asked in English, Sesotho and IsiZulu depending on what the participants were preferred to facilitate comprehension.

The interview schedule consisted of the following two main parts:

Part One: Demographic information, medical and psychological

This section was designed to include all the biographical and medical information pertaining to the client. Included in this section was the participant's age to ensure that the

participants fell within the inclusion criteria. Address and contact information was also included so as to allow for ease of follow-up for post-treatment assessment. The CD4 count was included to document progression of the disease and also to ensure that participants fell within the required guidelines regarding eligibility for ARV therapy. It was considered important to know the participant's medication and ART regime because some prescribed medications/ARV could have produced side effects that might have further exacerbated confusion or prevented the participant from continuing to participate in the study. All opportunistic infections that the participant presented with were documented so that any possible associations with cognitive and linguistic difficulties could be identified.

Part Two: Reported cognitive and language problems

Memory: This section asked questions related to whether participants experienced difficulty remembering everyday activities such as taking medication, turning off lights, stoves, etc., paying bills, and where they placed things like keys. This section included both open and closed ended questions. The section also asked participants what they did to remember, such as "Do you rely on other people?", "Do you write things down?", and "Do you keep all the information in your head?" The maximum and minimum possible scores for this section when closed ended responses are tallied are 13 and zero respectively.

Attention: This section was divided into three aspects of attention – internal distracters, external distracters and sustained attention. Questions on internal distracters focused on eliciting information related to how internal factors such as pain, psychological and emotional states were affecting their ability to perform activities of daily living. Questions asked included – Do you experience: feeling tired (describe); headaches (describe); pain (describe); sadness,

tearful (describe). Questions on external distracters focused on eliciting information related to how external forces such as noise, voices and movement within the participant's immediate environment might interfere with attending to activities of daily living. Sustained attention questions focused on whether individuals exhibited difficulties staying focused or interested in an activity for an extended period of time. Activities included listening to what doctors or nurses said, listening to a telephone conversation, being interested in a task for more than an hour. The maximum (max) and minimum (min) possible scores for this section when closed ended responses were tallied:

- Attention internal distractors –zero (min) and 13(max)
- Attention external distractors- zero (min) and three (max)
- Sustained attention – zero (min) and five (max)

Visual: This section asked questions that elicited information on whether participants presented with visual problems (or not) that may have affected their ability to perform activities of daily living such as seeing objects in the distance or seeing spots when looking at something. Questions pertaining to problems with vision were included, such as burning eyes, painful eyes, spots when looking at something; and headaches even though it is acknowledged that visual spatial or visual processing is a higher order mental process. Part of processing visual information involves information received from the senses, namely the eye. The maximum and minimum possible scores for this section when closed ended responses are tallied are six and zero respectively.

Executive functions: This section asked questions related to whether participants experienced difficulty with adding up, making a decision, starting or completing a task, recognizing mistakes and correcting them. Participants were asked to solve a problem by providing two solutions. The maximum and minimum possible scores for this section when closed ended responses are tallied are eight and zero respectively.

Language: This section asked questions that included information about the participant's hearing, expressive and receptive language abilities that may have been affecting their abilities to participate in activities of daily living. Part of processing information involves sensory information hence information regarding hearing was elicited even though the ability to process auditory information requires higher order mental processes. Hearing questions included: "have you ever had a hearing test?" "Do you hear things only when they are loud?" Expressive language included questions such as "Do you have difficulty: talking for a long period; spelling words, starting a conversation and maintaining a conversation?" Receptive questions included: "Do you have to ask people to repeat themselves when talking?" "Do you have difficulty: remembering what someone has asked you; remembering what the doctor or nurse said?" The maximum and minimum possible scores for this section when closed ended responses were tallied:

- Receptive language - seven (max) and zero (min).
- Expressive language - seven (max) and zero (min).

Interpersonal difficulties pertaining to cognitive and language problems*:* This information was elicited to determine what possible cognitive and language problems were impacting on the

participants' abilities to interact and participate in activities. Questions included coping issues such as how does their diagnosis affect relationships with other people. The maximum and minimum possible scores for this section when closed ended responses are tallied are seven and zero respectively. For a summary of the participants' maximum and minimum performance refer to Table 5.11. Table 4.7 sums up the questions and variables that the structured interview schedule serves to investigate.

Table 4.7 Variables, Research Questions and Sections pertaining to the Structured Interview Schedule

Variable Name	Research question	Sections on the Interview schedule
Independent variable Age, CD4 count, ARVs, education, gender – nominal	What independent variables affect cognition and language	Items under demographic, medical and psychological section
Dependant variable Cognitive abilities – nominal Open ended questions	Do adults living with HIV and or AIDS present cognitive deficits and do these affect activities of daily living	Items pertaining to memory attention, vision, visual spatial and executive functions sections
Dependant variable Language –nominal Open –ended questions	Do adults living with HIV and or AIDS present language deficits and do these that affect activities of daily living	Items pertaining to hearing, expressive and receptive language sections

4.6 Procedure

The experimental and comparison group were followed up at four-monthly intervals (baseline, four and eight months). These intervals were chosen because they coincided with the participants' medical check-up. This was done to reduce attrition and ensure that patients would not incur extra costs in order to participate in the study. In other words, this study was conducted in three phases that included the baseline, four and eight months. In the baseline phase, the experimental group and comparison group were assessed using the Cognitive Linguistic Quick Test and were asked questions regarding their ability to perform activities of daily living. At baseline the participants in the experimental group had not initiated HAART. At four months (Phase 2) the same participants from the experimental and comparison group were re-assessed. The only difference was that the experimental group had now been on HAART for four months. For the cross-sectional group, another cohort of participants was recruited and tested. At eight months the experimental and comparison group were retested and another new cohort of participants was recruited for the cross-sectional group.

Pilot study

Prior to the commencement of the study a pilot study was conducted using the Cognitive Linguistic Quick Test and interview schedule. The pilot study was described in great detail in chapter three.

Experimental group testing procedures.

Phase 1: Baseline study procedures.

Permission was obtained from the relevant authorities to conduct the study. This included the superintendent of the hospital, and the director of the clinical HIV research unit at the clinic who oversees all research conducted at the clinic (refer to Appendix II). Once permission was obtained, the researchers then approached the head doctor and nurse at the clinic to inform them that permission had been obtained from the relevant authorities and to tell them about the study. The nurse in charge then proceeded to tell the researcher about when and how to recruit the participants for the study.

Participants were recruited from the wellness and adherence counselling programme. Before patients start the ARV drugs, they have to go through a series of counselling programmes and one of them is the wellness and adherence programme. Patients arrive very early for this counselling programme which starts at 9 am. This programme is usually presented in a large classroom. The researcher along with the research assistants would be in the classroom between 7.30 am and 7.45 am and give a presentation about the purpose and description of the study, the basis for selection of the participants, and an explanation of the procedures. The patients were then invited to participate in the study. The consent form was explained and elaboration provided if needed. Informed consent is "the contractual obligation" in research. Informed consent reflects the understanding of the participants regarding what the study involves (Rosnow & Rosenthal, 1997). Written permission to be tested was obtained from the subjects with an understanding that their confidentiality would be maintained and that they could withdraw from the study at any time (refer to Appendix III). The patients that volunteered were than led out of the classroom into the quiet quadrangle area where testing occurred. The garden quadrangle at the clinic is very large with three long tables and benches.

The tables were moved far away from each other so that participants could not hear each other's responses. A participant and examiner sat at each table facing each other. Three trained research assistants administered the test and conducted the interview. The research assistants were also able to translate the questions into the vernacular, namely IsiZulu and Sesotho, to facilitate comprehension of the questions. (Please see Pilot study chapter 3 - on how test was translated section 3.2.3). The participants were also given the option of conducting the test in English. The participants were provided with a pen or pencil to perform the written tasks. The Cognitive Linguistic Quick Test took approximately 30 to 40 minutes to complete. The survey was conducted face to face and took approximately 25 minutes to complete.

Phase 2: Four months post-baseline

Patients who enrolled at the clinic are made aware of the fact, that the clinic is affiliated to a research unit (Clinical HIV Research Unit) and that any information collected will be used for research purposes. All patient information is collected and inputted into a database. From this data base the researcher was able to identify when participants were due back for their four month visit.

Four months was chosen because this is the time the participants were required to come and refill their prescription for ARVs at the clinic. They were given a set date to come to the clinic. The researcher felt that it would be easier to retest the participants when they had to come to the clinic, rather than asking them to come to the clinic on a day that was not scheduled for an appointment. The research assistants would call the participants to remind them of the study and arrange a place to meet them at the clinic, when they came for their four month refill of ARVs. Testing then proceeded as in phase 1.

Phase 3: 8 -10 months post-baseline

From the data base the researcher was able to identify the scheduled dates when participants were due back for their eight month visit. The research assistants (RAs) would call the participants to remind them of the study and arrange a place to meet them in the clinic. Testing then proceeded as in phase 1.

Comparison group testing procedures.

Not all HIV-positive patients registered at the out-patient clinic were on ARVs for several reasons. Some patients elect not to go on ARVs because of the reported side effects. Others elect not to go on ARVs because they are asymptomatic and feel fine. However, most of the patients were not on ARVs because their CD4 counts were too high for initiation of treatment according to the WHO recommendations at the time when recruitment started. At the clinic there was a room devoted to patients who were not on ARVs where they came in for counselling and medical check-ups. In an effort to increase participant recruitment, the clerk in charge of the files was approached to provide information pertaining to patients who were not receiving ARVs. The clerk provided the researchers with the times that patients would come in for CD4 counts and medical check-ups. Participants were then approached while they waited for their medical check-ups. Ethical and testing procedures were then adhered to as in the case with the experimental group.

Cross-sectional testing procedures

Participants were recruited from the database at the clinic. The researcher approached the clerks overseeing the database to obtain information about the patients. This information included patient name, contact information, scheduled date for refill of ARVs at four months and eight months, presenting illness and treatment regimen. Once this information was collected, the researcher and the research assistant called patients and invited them to participate in the study. A date, time and place at the clinic were scheduled for the patient to meet with the researchers. This was done again at four and eight months using the same procedure as aforementioned. The only difference was that the researcher asked the database clerk for information pertaining to individuals who had either taking HAART for four or eight months.

4.7 Ethical Considerations

This research was submitted to the University of Witwatersrand University Medical Ethics Committee. A clearance certificate was granted on 2 March, 2007, with the protocol number M070201 (see Appendix I).

Permission to conduct the study was obtained from the Head of Clinical HIV Research Unit affiliated with the HIV out-patient clinic (see Appendix II). Informed and written consent was obtained from the participants (see Appendix III). Contribution to the transport costs was made to the participants at each visit. Once permission to conduct the research was granted, the ethical principles of confidentiality, autonomy, beneficence, non-maleficence, and justice were adhered to.

Confidentiality.

Participants were informed that their identities would be kept confidential in that they would not be published or disclosed to third parties. Confidentiality was further ensured by coding names and keeping all response sheets and transcripts under lock and key in the researcher's office. The information would also be destroyed five years after completion of the study. In AIDS research there is a need to balance confidentiality against the need to develop appropriate information.

Autonomy.

It was emphasized that participants were under no obligation to participate in the study and that participation was voluntary. They were informed that they could withdraw from the study at any stage without any negative consequences. They were also told that they were under no obligation to answer all the questions, and they could choose not to answer all or specific questions during the interview process.

Beneficence and non-maleficence.

Direct benefits or risks to the patient were seen as minimal as the information obtained was not going to necessarily benefit the participants but would have direct benefits for prospective patients at the clinic. The information being obtained had direct implications for the clinical management of patients and research as both these areas rely on neurocognitive data to generate clinical classifications of impairment (Singh et al., 2010). The only risk participants

were likely to face would be to lose their place in the queue for medical consultations or counselling appointments.

Justice.

The participants in this study were considered a vulnerable population. They were considered vulnerable due to the fact that HIV and AIDS is an on-going condition that can adversely affect a person's cognitive abilities and psyche. However, the exclusion criteria ensured that HIV-positive individuals showed adequate understanding to provide consent (Moser et al., 2002). Therefore, based on the fact that the majority of participants came to the clinic unaccompanied and used public transport, it was felt that the patients were able to provide informed consent.

4.8 Reliability and Validity

4.8.1 Pilot Study

The pilot study was conducted to identify any potential problems with data collection and to demonstrate that the design was appropriate and feasible. The Cognitive Linguistic Quick Test and the structured interview schedule were pre-tested on a small sample of participants with similar characteristics to the target sample. The procedure and results were discussed in chapter 3. It was important that the interview schedule be piloted to make sure that items measured what they were supposed to, i.e. exhibited face validity (Babbie & Mouton, 2001).

The CLQT was developed to assess the cognitive and linguistic functions of adults (18-89 years old) with suspected neurological dysfunction as a result of strokes, traumatic brain injury or dementia. (Helm-Estabrooks, 2001). This test has been used in previous studies to determine the cognitive abilities of individuals with Parkinson's disease (Parashos, Johnson, Erickson-Davies & Wielinski, 2009) and high level cognition-based communication disorders in mild traumatic brain injury (Blyth, Bond, Scott & Farquhar, 2010). Due to the fact that the CLQT had not been used on a South African population with suspected neurological dysfunction, a pilot study was conducted. The pilot study determined that the CLQT could be used on a South African population living with HIV and AIDS.

Further reliability for the open-ended questions of the interview schedule was determined by asking another independent rater, a qualified speech language pathologist, to analyse 25% of the interview schedules to make sure the same themes were identified as those identified by the researcher were identified by the rater, thereby ensuring inter-rater reliability. An agreement of 97% was achieved, ensuring inter-rater reliability. Based on this finding from the pilot study the interview schedule was used in this study.

4.8.2 Cognitive Linguistic Quick Test

Intercorrelations of the cognitive domains scores for both the CLQT and the interview schedule were done and are shown in Table 5.4. All five of the cognitive domains on the CLQT significantly correlated with each other, ranging from r=0.3 to r=0.87. On the Interview schedule most of the domains are significantly correlating except for executive function with memory, visual spatial and attention. The strongest correlation was executive function with language explaining greater than 50% of the variability (r=0.87, $r^2=0.87^2$= 76% of the variability). However there were few weak significant correlations (e.g visual spatial [CLQT] with executive functions [IS] r=.22, $r^2 = 0.22^2 = 0.05$% of variability). Therefore domains from

each instrument were independent, demonstrating divergent validity. That is even though both tests were looking at the same phenomena-cognitive linguistic abilities, they basically were testing different aspects - one was looking at impairments and the other activities of daily living as purported in the ICF model of disability.

Table 4.8 Correlations of the Cognitive Domain scores for the CLQT and Structured Interview Schedule

	Executive Functions (IS)	Memory (IS)	Visual Spatial (IS)	Language (IS)	Attention (IS)	Executive Functions (CLQT)	Memory (CLQT)	Visual Spatial (CLQT)	Language (CLQT)	Attention (CLQT)
Exec. Funct (IS)	**1.00**									
Memory (IS)	**0.43*** **									
Vis. Spatial (IS)	-0.02	**0.22*** **								
Language (IS)	**0.75*** **	**0.49*** **	**-0.13***							
Attention (IS)	**0.73*** **	**0.49*** **	**-0.12***	**0.89*** **						
Exec. Funct (CLQT)	**0.17** **	0.03	0.09	**0.15** **	0.1					
Memory (CLQT)	0.09	0.08	0.1	0.05	0	**0.39*** **				
Vis. Spatial (CLQT)	**0.22*** **	0.07	**0.12***	**0.12***	0.07	**0.74*** **	**0.45*** **			
Language (CLQT)	0.06	0.03	0.03	0.08	0.04	**0.42*** **	**0.70*** **	**0.30*** **		
Attention (CLQT)	**0.21*** **	0.07	0.08	0.15*	0.1	**0.62*** **	**0.39*** **	**0.87*** **	**0.35*** **	**1.00**

p = < .05* p= <.01 ** p= <.001 ***

The reliability of the Cognitive Linguistic Quick Test and the interview schedule were established to determine internal consistency using the Chronbach Alpha. According to Spiliotoulou (2009) internal consistency refers "to whether participants are responding to the different items of a questionnaire in a consistent manner in a single trial" (pp.3). The most widely accepted indicator of internal consistency is the Chronbach alpha.

The reliability of the measures used in this study was established to determine the degree to which the items of the CLQT and interview schedule examined the same construct (de Vos, Strydom, Fouché & Delport, 2005). The internal consistency of the Cognitive Linguistic Quick Test (CLQT) and the interview schedule (IS) was calculated by looking at each group at the different time periods and by combining the responses from the participants in the experimental, cross-sectional and control group together. It was important to explore the internal consistency of both measures since both tests had not been standardized on a South African cohort. The reliability coefficients are presented in Table 4.9 according to the instruments used in this study.

Table 4.9 Internal Consistency Reliability Coefficients for the CLQT and IS according to Group Performance at Baseline, Four and Eight months.

Group	Instrument	Base	4 months	8 months
Experimental	CLQT	0.8	0.74	0.76
	IS	0.96	0.94	0.9
Comparison	CLQT	0.84	0.91	0.88
	IS	0.72	0.79	0.55
Cross-sectional	CLQT	0.69	0.82	0.74
	IS	0.94	0.84	0.68

From Table 4.9 one can see that the groups appear to be responding differently according to the instrument. The experimental and cross-sectional groups are responding in a similar manner which is different from comparison group. Conventionally, reliability estimates of 0.70 are acceptable (Huck, 2008). According to (Spiliotoulou, 2009), it is not unusual for tests in the therapy disciplines to exhibit Cronbach's alphas that are lower than 0.7 as seen with values of 0.55, 0.68 and 0.69. The low values could have been due to several factors. A few of the subsections on the CLQT and interview schedule had few items assigned to them. In addition, sample size has been noted to affect internal consistency, for example the n=9 at baseline for the comparison group (Cortina, 1993; Spiliotoulou, 2009). Based on the latter, the reliability estimates presented in Table 4.10 were deemed acceptable for this study.

Table 4.10 Internal Consistency Reliability Coefficients for the CLQT and IS according to group performance

Instrument	Experimental N=161	Comparison N=40	Cross-sectional N=138
CLQT	0.78	0.88	0.80
IS	0.95	0.74	0.93

The results in Table 4.10 revealed that the experimental and cross-sectional groups responded in a similar manner. All the reliability estimates were above 0.70, which was deemed acceptable for this study (Huck, 2008).

4.8.2 Interview Schedule

Validity was further established through trustworthiness. Trustworthiness was determined through the process of triangulation, peer debriefing and the use of direct quotes. Triangulation refers to the use of both quantitative and qualitative methods that form a persuasive conclusion and enhance concurrent validity (Wilkins & Woodgate, 2008). The two approaches used in this research included a standardized test (CLQT) and an interview schedule. Peer debriefing was also used which "is the process of exposing oneself to a disinterested peer in a manner paralleling an analytical session and for the purpose of exploring aspects of inquiry that might otherwise remain implicit within the inquirer's mind" (Cohen & Crabtree, 2008, p. 4). This was done to reduce the effects of reactivity and bias (Leitz, Carol, Langer & Furman, 2006). In an attempt to remain true to the participants' perspective, direct quotes were used to reduce bias from the researcher.

In qualitative research generalization is referred to as transferability. Transferability is said to occur when findings from one setting can be transferred to similar situations or participants (Holloway & Fulbrook, 2001). From a qualitative perspective, transferability is primarily the responsibility of the individual doing the generalizing. To ensure transferability of the findings, the researcher described in detail where the research took place, instrumentation, as well as the ethical and research procedures that were employed to conduct the research. Furthermore, the researcher made her assumptions implicitly and explicitly known such as that HAART would improve the cognitive-linguistic abilities of individuals living with HIV and AIDS and participants would exhibit cognitive-linguistic deficits due to disruptions of the fronto-striatal circuitry (Holloway & Fulbrook, 2001).

As pertaining to the pilot study, reliability for the open-ended questions of the interview schedule was determined by asking another independent rater, a qualified speech language pathologist, to analyse 25% of the interview schedules to make sure the same themes were identified as those identified by the researcher were identified by the rater, thereby ensuring inter-rater reliability. An agreement of 97% was achieved, ensuring inter-rater reliability.

4.9 Power Analysis

An apriori power analysis was conducted holding α at 0.05 and β at 0.80. For the repeated measures ANOVA testing differences (using the ratio one in theexperimental and one in the comparison group), a minimal sample size of 28 would be required to detect medium effect sizes (0.25). This suggests that the current sample size was adequate to test the research hypotheses (given a sample of over 50 across the three testing periods).

4.10 Data Analysis

4.10.1 Preliminary Analysis

Preliminary analysis was conducted to determine the reliability, validity and intercorrelations, of the instruments. In addition descriptive statistics were also done to identify any trends that could emerge from form the instruments.

The reliability of the CLQT and interview schedule were assessed using the Cronbach's alpha to determine internal consistency. The validity of the two instruments was checked by determining the construct validity through exploratory factor analysis. All reliability and validity procedures and statistics are reported in the results chapter. Intercorrelations were conducted between the dependant variables (cognitive domains) on the CLQT and interview schedule. Overall there were significant correlations observed with the five cognitive domains in each instrument and between each instrument.

Descriptive statistics were used to summarize and reveal patterns that emerged (Bordens and Abbott, 2011) from the performance of the participants in the experimental, cross-sectional and control group on the Cognitive Linguistic Quick Test (CLQT) and the interview schedule. The raw scores on the CLQT were tallied for each task and cognitive domain. The composite score for each cognitive domain was determined to provide an overall severity rating of the individual's performance at the three times of testing. The severity ratings for all the cognitive domains were determined by matching the participants' composite score with the ranges of severity as shown on the CLQT (see Appendix V).

Severity ratings are important in terms of clinical performance in the profession of speech language pathology. Hence severity ratings were computed for this study. For the

interview schedule all the responses for closed-ended questions were tallied to obtain the raw scores for each subtest and cognitive domain. The measure of central tendency (mean) and spread of variance (standard deviations) were calculated for the individual tasks and cognitive domains on the CLQT and interview schedule across all three groups at baseline, four and eight months. The median was also calculated for the cognitive domains. The severity ratings for all the cognitive domains were also determined by matching the participants' cognitive domain score with the ranges of severity as shown on the CLQT (see Appendix V).

4.10.1 Main analysis

Inferential statistics allowed for the inferences to be made from a sample recruited for this study drawn from the population of urban South African individuals living with HIV and AIDS (Bordens & Abbott, 2011). Inferential statistics were done on both the CLQT and the interview schedule. Even though the interview schedule brought a qualitative flavor to the design, it was able to provide quatitive information from the closed ended questions when responses were tallied up and raw scores obtained. Before the main analysis could be done parametric assumptions were tested for the all the inferential statistics used.

A Kruskal – Wallis test to determine whether a difference in cognitive-linguistic ability existed between the three groups at baseline, four months and eight months. Post hoc analysis included a pairwise test. To analyse whether there was a significant difference in cognitive-linguistic abilities within the participants (time effect) for the experimental and comparison groups, a one-way repeated measures analysis of variance (RM- ANOVA) was used. Post testing included a paired – test for repeated measures to determine where significant differences lay between within subjects in a group at a particular time. To determine whether

age, education, CD4 counts and gender had an (within and between subject) effect on the cognitive-linguistic functioning in both the experimental and comparison groups at the three testing periods a repeated measures Analysis of Covariance (ANCOVA) was used. Three co-variance structures were run with three goodness of fit statistics. The co-variance structures or models included Compound symmetry, Huynh-Feldt and Autoregressive (1). The three goodness of fit statistics used included the Akaiake information criteria (AIC), Corrected Akaiake information criteria (AICC) and Bayesian information criteria (BIC).

The data collected from the structured interview schedule was analysed both quantitatively and qualitatively. Content analysis was used to address the fourth aim which set out to investigate whether cognitive linguistic abilities affect the performance of activities of daily living. To address this aim, the closed- and open-ended questions were thus analysed by means of quantitative and qualitative content analysis. Categories were predetermined based upon prior research and theory. The transcripts were coded within the predetermined themes. These codes were then used to determine the frequency of responses to the themes (categories) and sub-themes. Any text that could not be categorized under the sub-themes was given a code of "other" (Hsieh & Shannon, 2005). Table 4.11 summarizes the aims, hypothesis variables and assumptions under investigation in this study.

Table 4.11 Aims, Variables, Analysis and Assumptions addressed in this Research

Aims	Variables and properties	Analysis and assumptions
1. To determine whether there is a significant difference in cognitive-linguistic abilities between the experimental, comparison and cross-sectional groups on the Cognitive Linguistic Quick Test and the interview schedule. *Hypothesis:* There are significant differences in cognitive linguistic performance between the groups	-*Independent variables* Experimental group, Comparison group and Cross sectional -*Dependant and interval variables at each testing period*: Attention, Memory, Executive function, Language, Visual spatial	Kruskal – Wallis was used to determine between group differenced Post hoc analysis included Pair-wise testing
2. To determine whether there will be a significant difference in cognitive-linguistic abilities within the participants (time effect) for the experimental and comparison groups on the Cognitive Linguistic Quick Test and the interview schedule. *Hypothesis:* There are	-*Independent variables:* Experimental group and Comparison group *Dependant and interval variable:* Attention Memory Executive function Language Visual spatial	One way Repeated Measures: Anova Tested for Assumption of Sphericity and the other assumptions were verified from the previous analysis. For within group analysis the repeated measures analysis of variance was used Post hoc analysis included paired t-test to determine the significance between two related samples.

significant within group differences in cognitive linguistic performance across the three testing times.		
3. To determine the effect of age, gender, education and CD4 count on cognitive-linguistic functioning in both the experimental and comparison groups at baseline, four months and eight months on the Cognitive-Linguistic Quick Test and the interview schedule. *Hypothesis:* The variables of age, gender, education and CD4 count have a significant effect on cognitive –linguistic abilities.	*Independent variables:* Age, education, CD4 count – continuous Gender - categorical *Dependant variables* Time and group *Covariances* Attention Memory Executive function Language Visual spatial	ANCOVA Assumption of sphericity and the other assumptions were verified from the previous analysis, coupled with residual analysis of model fit. The structure of the temporal random effects was modelled using three different approaches and the model goodness of fit was used to select the best fitting model.
4. To describe the cognitive-linguistic abilities that affect performance and activities of daily living in the experimental, cross-sectional and control groups. *Question:* Do cognitive – linguistic abilities affect activities of daily living.	Independent variables: Testing periods Groups Dependant variable: Attention Memory Executive Function Language Visual Spatial	Quantitative and qualitative Content Analysis: Pre - determined Categories: Attention Memory Executive Function Language Visual Spatial

In summary the study examined the effect of HAART on the cognitive – linguistic abilities of individuals living with HIV and AIDS. The research design predominately was quantitative in nature except for the open ended questions included in the structured interview schedule which provided a minor qualitative flavour to the study. The responses from the structured interview were meant to compliment the findings obtained from the CLQT. Three groups of participants were recruited to participant in this research – experimental, comparison and cross sectional comparison group. A cross sectional comparison group was recruited because of the high attrition rate observed after baseline testing and the low numbers of participants in the comparison group. The comparison group consisted of individuals who were HIV positive and had also elected not to take HAART. The two measures administered in the study were described in this chapter and rationales for both their inclusion were indicated in the literature review section 2.7.3.1. The results from the pilot study facilitated the use of the Cognitive Linguistic Quick Test and the structured interview schedule in the main study. The pilot study highlighted the possible challenges to the main study. The pilot study allowed the researcher to find a more efficient way of recruiting participants. It also showed that the Cognitive Linguistic Quick Test could be used on a South African population, and be translated into the vernacular without losing face validity. The pilot study also permitted the researcher to slightly adjust the questions in the interview schedule and thereby reduce redundancy. In addition, ethical procedures, reliability and validity were taken into consideration so that the results from this research could be replicated. Lastly the data were analysed using both descriptive and inferential techniques.

Chapter 5: Results

5.1 Introduction

The primary aim of the study was to investigate the effects of HAART on the cognitive-linguistic abilities of adults living with HIV and AIDS before and after HAART initiation. A predominantly quantitative approach embedded with an interview schedule in order to obtain a broader understanding of the effects of HAART on the cognitive-linguistic abilities of adults living with HIV and AIDS. The study was both longitudinal and cross-sectional to determine the effects of HAART and also to establish preliminary trends in the description of cognitive-linguistic abilities in adults living with HIV and AIDS. Furthermore, the study also investigated how cognitive-linguistic abilities impact upon the ability to perform activities of daily living.

5.2 Preliminary Analysis

5.2.1 Parametric assumptions.

At each of the testing time points the participants were believed not to have violated the assumption of iid (independently and identically distributed) assumption. It was also assumed the participants recruited for the experimental, comparison group and cross-sectional were independent samples. In addition it was also assumed that the participants' data observed over time correlated (not independent) except those for the cross-sectional group which was comprised of different participants at each testing period.

Normal distribution

The following assumption was tested - that the scores for the cognitive domains would be normally distributed. Normal distribution was investigated with reference to skewness, the Kolmogorov-Smirnov test, the Shapiro - Wilks and histograms (refer to Appendix VII). When the skewness values fell between +1 and -1 they were considered to be normally distributed (Fife-Schaw, 2010). Values of $p > 0.05$ on the Kolmogorov-Smirnov test and the Shapiro – Wilks were considered to be normally distributed, and these values ultimately determined whether the domain(s) was normally distributed since they are more sensitive.

Cognitive Linguistic Quick Test (CLQT)

The data was assessed for normality of distribution for each group at baseline, four months and eight months.

Table 5.1 Tests of Normality for the CLQT for the Experimental, Comparison and Cross Sectional Groups

		Baseline			4 months			8 months		
Group	**Domains**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**
Experimental	Attention	-0.77	0.02*	0.00*	-1.43	<0.01**	<0.01**	-1.37	<0.01**	<0.01**
	Memory	0.01	0.14	0.07	0.55	>0.15	0.19	-0.02	>0.15	0.13
	Exec. Functions	-0.13	>0.15	0.22	-0.37	0.03*	0.05	-0.31	0.07	0.23
	Language	0.14	0.13	0.47	0.13	>0.15	0.42	0.16	>0.15	0.43
	Visual Spatial	-0.18	>0.15	0.09	-0.75	>0.15	0.01*	-0.87	<0.01**	0.00**
Comparison	Attention	-0.45	0.05	0.07	-1.19	>0.15	0.25	-0.76	>0.15	0.26
	Memory	-0.47	0.07	0.2	0.69	>0.15	0.49	-1.32	>0.15	0.26
	Exec. Functions	-0.15	>0.15	0.31	-0.66	>0.15	0.73	-0.19	>0.15	0.47
	Language	-0.13	>0.15	0.82	0.36	>0.15	0.66	-0.77	>0.15	0.81
	Visual Spatial	-0.63	>0.15	0.28	-1.48	<0.01**	0.05	-0.93	0.14	0.09
Cross sectional	Attention	-1.29	<0.01**	<0.01**	-1.76	<0.01**	<0.01**	-2.90	<0.01**	<0.01**
	Memory	-0.96	<0.01**	<0.01*	-0.17	>0.15	0.62	-0.42	>0.15	0.07
	Exec. Functions	-0.27	>0.15	0.67	3.09	<0.01**	<0.01**	-1.03	<0.01**	0.01*
	Language	-0.28	<0.01**	0.06	-0.36	<0.01**	0.05	-0.58	0.05	0.26
	Visual Spatial	-0.67	0.02*	0.03*	-1.25	<0.01**	0.00**	-1.60	0.02*	<0.01**

Kolm. Smir = Kolmogorov-Smirnov test, p<.05*. p<.01.**

Tests of normality data (Table 5.4) revealed that all the cognitive domains for the experimental group were normally distributed except for attention at baseline, and attention and executive function at four months. At eight months all were normally distributed except for language and visual spatial. For the comparison group, all the domains were normally distributed for all the testing periods except for visual spatial at four months. Results for the cross-sectional group revealed that the executive function to be normally distributed at baseline, language and memory were normally distributed at four and eight months.

Interview Schedule (IS).

The data was assessed for normality of distribution for each group at baseline, four months and eight months.

Table 5.2 Tests of Normality for the IS for the Experimental, Comparison and Cross Sectional Group

		Baseline			4 months			8 months		
Group	**Domains**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**	**Skewness**	**Kolm. Smir**	**Shapiro-Wilks**
Experimental	Attention	-1.42	<0.01**	<0.01**	-2.30	<0.01**	<0.01**	-2.33	<0.01**	<0.01**
	Memory	-0.92	<0.01**	0.00**	-1.45	<0.01**	<0.01**	-1.55	<0.01**	<0.01**
	Exec. Functions	-1.69	<0.01**	<0.01**	-1.82	<0.01**	<0.01**	-2.14	<0.01**	<0.01**
	Language	-1.78	<0.01**	<0.01**	-1.63	<0.01**	<0.01**	-1.77	<0.01**	<0.01**
	Visual Spatial	-1.39	<0.01**	<0.01**	-2.20	<0.01**	<0.01**	-1.08	<0.01**	<0.01**
Comparison	Attention	0.18	>0.15	0.1	0.47	>0.15	0.72	-0.96	0.05	0.1
	Memory	-1.49	<0.01**	<0.01**	-1.52	<0.01**	0.00**	-1.92	<0.01**	0.00**
	Exec. Functions	-1.46	<0.01**	<0.01**	-1.18	<0.01**	0.00**	-1.01	<0.01**	0.00**
	Lanaguage	-2.34	<0.01**	<0.01**	-1.16	0.03*	0.01*	-2.11	0.04*	0.00**
	Visual Spatial	-2.83	<0.01**	<0.01**	-0.86	0.02*	0.02*	-1.19	<0.01**	0.00**
Cross sectional	Attention	-0.67	<0.01**	0.02*	-1.15	0.01*	0.00	-0.88	<0.01**	0.00**
	Memory	-2.12	<0.01**	<0.01**	-3.14	<0.01**	<0.01**	-1.56	<0.01**	<0.01**
	Exec. Functions	-0.60	<0.01**	<0.01**	-2.47	<0.01**	<0.01**	-4.24	<0.01**	<0.01**
	Lanaguage	-1.08	<0.01**	<0.01**	-1.71	<0.01**	<0.01**	-1.27	<0.01**	<0.01**
	Visual Spatial	-1.04	<0.01**	<0.01**	-3.00	<0.01**	<0.01**	-2.30	<0.01**	<0.01**

Kolm. Smir = Kolmogorov-Smirnov test p<.05* , **p<.01**.

The statistical analysis shown in Table 5.5 revealed attention to be the only normally distributed domain for the comparison group. All other domains were not normally distributed for the cognitive domains across all the groups at the three different testing periods. This could have been due to the number of items per subtest of the schedule.

Homogeneity of Variance (between groups).

The Levene's test of homogeneity was conducted to verify the assumption of homogeneity of variance. The assumption was met when Levene's test yielded a p-value of >0.05.

Cognitive Linguistic Quick Test

Based on the the results depicted in Table 5.3 the assumption of homogeneity of variance was met for all the domains except for executive functions and language at baseline. At four months the assumption of homogeneity of variance was met for all the domains except for the language and visual spatial. At eight months the assumtion of homogeneity was met for the domains memory and language. The null hypthesis stating that there was homogenous variance in the data failed to be rejected, based on p-values greater than 0.05. Therefore the results were intepretated using the parametric statistics. Higlighted and bolded areas are significant

Table 5.3 Levene's Test of homogeneity for the experimental, comparison and cross sectional group on the CLQT

Cognitive domains	Baseline	Four Months	Eight Months
Attention	**0.06**	**0.24**	**0.71**
Memory	**0.09**	**0.16**	0.04
Executive Functions	**0.05**	**0.36**	**0.24**
Language	<.0001	<.0001	<.0001
Visual Spatial	**0.93**	**0.05**	**0.22**

Levene's p = >0.05

Interview Schedule

The results shown in Table 5.4 revealed that the assumption of homogeneity of variance was met for all the domains except for executive functions at baseline. At four months the assumption of homogeneity of variance was met for all the domains except for the language and visual spatial. At eight months the assumtion of homogeneity was met for the domains attention, executive function and visual spatial. The null hypthesis stating that there was homogenous variance in the data failed to be rejected based upon most of the domains exhibiting significant Levene's values. Therefore the results were intepretated using the parametric statistics.

Table 5.4 Levene's Test of Homogeneity for the Experimental, Comparison and Cross sectional group on the Interview Schedule

Cognitive domains	Baseline	Four Months	Eight Months
Attention	**0.08**	**0.19**	**0.77**
Memory	**0.09**	**0.34**	**0.07**
Executive Functions	0.00	**0.72**	**0.64**
Language	**0.06**	**0.52**	**0.08**
Visual Spatial	**0.18**	0.03	**0.30**

5.2.2 Descriptive Statistics

Overview of scores obtained on the Cognitive Linguistic Quick Test (CLQT)

Table 5.5 reflects the means, standard deviations and range of scores obtained by the three groups of participants. The participants in the three groups were noted to have the most difficulties with the tasks of story retelling, phonemic categorization, symbol trails and design generation.

Table 5.6 reflects an overview of the means, medians, standard deviations and range of cognitive scores obtained by the three groups of participants.

Table 5.5 Means, Standard Deviations and Range of Scores obtained by each Group on the CLQT Tasks

Tasks	Max. Possible score	Mean	STD	Range	Mean	STD	Range	Mean	STD	Range
Experimental		**Baseline (N=55)**			**4 months (N=55)**			**8 months (N= 51)**		
Personal Facts	8	7.91	0.35	6-8	7.96	0.27	6-8	8.00	0.00	8-8
Symbol Cancellation	12	9.18	4.30	0-12	10.25	3.24	0-12	10.69	2.53	2-12
Confrontational Naming	10	9.57	0.87	6-10	9.85	0.45	8-10	9.75	1.06	3-10
Story Trails	10	5.87	3.50	0-10	7.07	3.30	0-10	7.22	3.26	0-10
Symbol Retelling	10	6.95	2.11	2-10	7.29	1.89	4-10	7.76	1.85	4-10
Generative Naming	9	4.49	1.56	2-9	4.82	1.39	3-9	4.86	1.36	2-9
Design Memory	6	4.58	1.03	2-6	4.85	1.15	2-6	5.14	0.98	3-6
Mazes	8	4.35	2.97	2-8	5.80	2.26	0-8	6.02	2.08	1-8
Design Generation	13	4.27	2.26	0-8	5.05	1.76	1-9	4.98	1.73	1-10
Comparison		**Baseline (n=21)**			**4 months (n=10)**			**8 months (n= 9)**		
Personal Facts	8	7.95	0.22	8-8	7.50	1.27	4-8	8.00	0.00	8-8
Symbol Cancellation	12	10.24	2.96	0-12	11.70	0.95	9-12	12.00	0.67	12-12
Confrontational Naming	10	9.48	1.08	6-10	9.60	0.97	7-10	9.78	1.66	8-10
Story Trails	10	7.24	2.17	5-10	7.70	2.11	3-10	8.67	2.85	6-10
Symbol Retelling	10	5.81	3.30	2-10	6.80	3.71	0-10	7.89	1.69	3-10
Generative Naming	9	4.19	1.47	2-7	4.90	2.13	2-9	4.89	1.01	3-8
Design Memory	6	4.86	1.20	2-6	5.00	1.41	2-6	5.44	1.73	3-6
Mazes	8	5.43	2.38	0-8	5.90	3.35	0-8	7.00	2.29	4-8
Design Generation	13	4.24	2.59	2-10	4.30	2.26	0-8	6.33	57.13	3-11

Cross sectional		**Baseline (n=55)**			**4 months (n=43)**			**8 months (n= 39)**		
Personal Facts	8	7.48	1.08	4-8	7.81	0.85	0-8	7.79	1.28	0-8
Symbol Cancellation	12	9.41	4.34	0-12	10.05	3.75	0-12	10.56	3.45	0-12
Confrontational Naming	10	9.59	0.64	8-10	9.72	0.59	8-10	9.44	1.65	0-10
Story Trails	10	5.62	3.29	0-10	8.26	1.63	4-10	7.15	2.25	0-10
Symbol Retelling	10	6.20	2.47	0-10	7.98	3.04	0-10	7.33	3.34	0-10
Generative Naming	9	4.11	1.36	1-8	5.05	1.48	2-8	4.87	1.72	0-9
Design Memory	6	4.77	1.13	2-6	4.44	1.20	1-6	4.67	1.28	0-6
Mazes	8	4.95	2.83	0-8	5.60	2.53	0-8	5.79	2.09	0-8
Design Generation	13	4.00	2.30	0-9	5.26	2.40	0-10	5.44	2.20	0-10

Note: Minimum possible score on all tasks was zero

Table 5. 6 Means, Standard Deviations, Median and Range of Domain Scores obtained by each Group on the CLQT

	Max. Possible	Baseline (N=55)				4 months (N=55)				8 months (N= 51)			
Cognitive Domains	**score**	**Mean**	**Median**	**STD**	**Range**	**Mean**	**Median**	**STD**	**Range**	**Mean**	**Median**	**STD**	**Range**
Experimental			**Baseline (n=55)**				**4 months (n=55)**				**8 months (n= 51)**		
Attention	215	144	154	47	32-209	166	175	38	59-209	173	178	34	74-210
Memory	185	148	145	19	112-183	154	154	18	120-213	158	162	16	127-185
Executive Function	40	19	19	7	3-31	23	42	7	7-34	23	24	6	8-34
Language	37	29	29	3	20-36	30	29	3	24-36	30	30	3	25-37
Visuospatial	105	66	66	19	29-99	76	77	17	31-99	80	85	16	35-100
Comparison			**Baseline (n=21)**				**4 months (n=10)**				**8 months (n= 9)**		
Attention	215	161	171	37	36-205	183	185	24	130-210	193	198	17	164-213
Memory	185	147	156	22	114-183	158	164	19	123-185	166	171	19	125-189
Executive Function	40	20	21	8	11-32	24	25	7	4-35	26	27	6	17-34
Language	37	29	29	3	25-35	30	31	4	23-37	32	32	3	25-36
Visuospatial	105	73	75	20	25-92	83	89	19	38-100	87	88	14	64-103
Cross sectional			**Baseline (n=55)**				**4 months (n=43)**				**8 months (n= 39)**		
Attention	215	148	169	50	10-202	175	185	71	26-211	177	186	32	20-207
Memory	185	140	145	25	80-181	155	159	20	116-197	154	157	18	113-178
Executive Function	40	19	19	6	3-32	28	25	25	8-78	24	26	6	8-33
Language	37	28	28	4	18-37	31	31	3	25-36	30	31	3	22-37
Visuospatial	105	67	72	20	12-96	74	80	22	16-107	79	81	19	12-96

Note: Minimum possible score for all cognitive domains was zero

Severity Ratings on the CLQT

Even though the CLQT was shown to demonstrate appropriate reliability and validity for this study (see preliminary statistics section) it was with caution that these severity ratings were applied to this South African cohort since this test has not been standardised on a large HIV and AIDS population. Severity ratings have important clinical application in the profession of speech language pathology. Severity ratings are presented in Table 5.7

The severity ratings presented in Table 5.7 reveal that the worst severity rating was initially recorded at baseline for the executive functions for all the three groups. The participants generally exhibited difficulty with symbol trails, mazes and design generation - tasks that are heavily reliant on executive function, attention and visual spatial skills. The least affected cognitive-linguistic ability was language for all the groups. The participants did not demonstrate any difficulty in naming pictures of objects, and relaying personal facts. However, they did demonstrate mild difficulties with story retelling and verbal fluency that entailed phonemic categorization. Overall, at base line participants in all groups presented with global cognitive impairments ranging from severe to mild that either stayed the same or changed from four and eight months after taking HAART.

Table 5.7 Severity Rating of Cognitive Linguistic Abilities on the CQLT at Baseline, Four and Eight months for all Three Groups

Group	Cognitive Domains	Max. Possible Score	Mean	Severity	Mean	Severity	Mean	Severity
			Baseline (n=55)		**4 Months (n=55)**		**8 Months (n=51)**	
Experimental	Attention	215	143.67	Mild	166.02	Mild	173.08	Mild
	Memory	185	148.02	Mild	154.09	Mild	158.37	WNL
	Executive Functions	40	18.71	Mod	22.80	Mild	23.39	Mild
	Language	37	28.76	Mild	29.60	WNL	30.41	WNL
	Visual Spatial	105	65.89	Mild	76.29	Mild	80.22	Mild
			Baseline (n=21)		**4 Months (n=10)**		**8 Months (n=9)**	
Comparison	Attention	215	160.57	Mild	183.40	WNL	192.67	WNL
	Memory	185	147.24	Mild	158.40	Mild	166.33	WNL
	Executive Functions	40	20.00	Severe	23.90	Mild	25.56	WNL
	Language	37	28.71	Mild	30.10	WNL	31.67	WNL
	Visual Spatial	105	72.67	Mild	82.70	WNL	87.33	WNL
			Baseline (n=55)		**4 Months (n=43)**		**8 Months (n=39)**	
Cross-sectional	Attention	215	147.64	Mild	174.98	Mild	177.31	Mild
	Memory	185	140.41	Mild	154.81	Mild	153.87	Mild
	Executive Functions	40	18.68	Severe	28.44	Mild	24.46	Mild
	Language	37	27.79	Mild	30.67	WNL	30.21	WNL
	Visual Spatial	105	67.25	Mild	74.16	Mild	78.51	Mild

Mod=Moderate; WNL=Within Normal Limits

Overview of scores obtained on the Structured Interview Schedule (IS)

Table 5.8 reflects the means, standard deviations and range of scores obtained by the three groups of participants. The participants in the three groups were noted to have the most difficulties with the tasks of story retelling, phonemic categorization, symbol trails and design generation. Results indicated that the overall mean scores for the tasks and domains increased slightly from baseline, to four months and eight months.

Table 5.9 reflects an overview of the means, medians, standard deviations and range of cognitive scores obtained by the three groups of participants. Most of the mean scores were very close to the maximum score attainable for each task and cognitive domain except for language and attention.

Table 5.8 Means, Standard Deviations and Range of scores obtained by each group on the IS tasks

Tasks	Max. Possible score	Mean	STD	Range	Mean	STD	Range	Mean	STD	Range
Experimental		**Baseline (n=55)**			**4 months (n=55)**			**8 months (n= 50)**		
Memory	13	10.38	3.36	1-13	10.98	2.88	2-13	11.08	2.81	2-13
Att. Int Distraction	13	8.40	3.52	0-13	10.51	2.60	3-13	11.55	1.62	2-13
Att. Ext Distraction	3	2.51	1.00	0-3	2.71	0.88	0-3	2.98	0.14	0-3
Sustained Attention	5	4.38	1.24	2-5	4.53	1.30	3-5	4.88	0.52	0-5
Visual Spatial	6	4.78	1.62	1-6	5.00	1.69	0-6	5.59	0.92	0-6
Executive Function	8	6.02	2.70	0-8	7.11	1.75	1-8	7.29	1.75	0-8
Hearing	4	3.44	0.96	0-4	3.64	0.95	0-4	3.84	0.61	0-4
Expressive Language	7	5.89	1.78	1-7	6.69	0.74	2-7	6.96	0.20	0-7
Receptive Language	7	5.93	2.03	0-7	6.69	0.69	2-7	6.84	0.37	0-7
Comparison		**Baseline (n=21)**			**4 months (n=10)**			**8 months (n= 9)**		
Memory	13	11.95	1.50	8-13	12.10	1.37	9-13	12.22	1.39	9-13
Att. Int Distraction	13	8.43	3.03	4-13	8.10	2.88	4-13	9.78	2.17	5-12
Att. Ext Distraction	3	2.71	0.78	0-3	2.10	1.29	0-3	2.78	0.44	2-3
Sustained Attention	5	4.95	0.22	4-5	4.80	0.63	3-5	4.78	0.67	3-5
Visual Spatial	6	5.43	1.21	1-6	5.10	1.10	3-6	5.44	0.88	4-6
Executive Function	8	7.57	0.75	6-8	7.00	1.41	4-8	7.44	0.73	6-8
Hearing	4	3.86	0.48	2-4	3.50	0.85	2-4	3.89	0.33	3-4
Expressive Language	7	6.86	0.48	5-7	6.40	0.84	5-7	6.67	0.71	5-7
Receptive Language	7	6.90	0.30	6-7	7.00	0.00	7-7	6.44	0.73	5-7

Cross sectional		**Baseline (n=55)**			**4 months (n=43)**			**8 months (n= 39)**		
Memory	13	10.95	2.55	1-13	11.26	1.89	2-13	12.21	0.83	9-13
Att. Int Distraction	13	7.80	3.15	2-13	10.30	2.17	5-13	10.79	2.00	6-13
Att. Ext Distraction	3	2.36	1.09	0-3	2.81	0.63	0-3	2.97	0.16	2-3
Sustained Attention	5	4.29	1.29	0-5	4.88	0.50	2-5	4.97	0.16	4-5
Visual Spatial	6	4.36	1.89	0-6	5.67	0.87	2-6	5.79	0.47	4-6
Executive Function	8	5.34	2.97	0-8	7.07	2.03	0-8	7.49	1.43	0-8
Hearing	4	3.20	1.17	0-4	3.86	0.41	0-4	3.77	0.63	1-4
Expressive Language	7	5.48	1.93	0-7	6.53	1.05	2-7	6.31	0.89	4-7
Receptive Language	7	5.50	2.10	0-7	6.74	0.69	2-7	6.51	0.68	5-7

Att.Int = Attention Internal; Att. Ext=Attention External
Note: Minimum possible score on all tasks was zero

Table 5.9 Means, Standard Deviations, Median and Range of Domain Scores obtained by each Group on the IS

Cognitive Domains	Max. Possible score	Mean	Median	STD	Range	Mean	Median	STD	Range	Mean	Median	STD	Range
Experimental		**Baseline (n=55)**				**4 months (n=55)**				**8 months (n= 51)**			
Memory	13	10.38	9.00	3.36	8-13	10.98	11.00	2.88	3-13	11.08	10.00	2.81	2-13
Attention	21	15.29	14.00	5.02	3-21	17.75	14.00	4.20	7-21	19.41	14.00	1.87	3-21
Visual Spatial	6	4.78	6.00	1.62	1-6	5.00	6.00	1.69	0-6	5.59	6.00	0.92	0-6
Executive Function	8	6.02	8.00	2.70	0-8	7.11	8.00	1.75	1-8	7.29	8.00	1.75	0-8
Language	18	15.25	20.00	4.06	4-18	17.02	20.00	1.89	7-18	17.65	20.00	0.82	3-18
Comparison		**Baseline (n=21)**				**4 months (n=10)**				**8 months (n= 9)**			
Memory	13	16.10	13.00	2.95	0-13	12.10	13.00	1.37	9-13	12.22	13.00	1.39	9-13
Attention	21	5.43	16.00	1.21	12-21	15.00	14.00	3.43	10-21	17.33	18.00	2.45	13-20
Visual Spatial	6	7.57	6.00	0.75	1-6	5.10	5.50	1.10	3-6	5.44	6.00	0.88	4-6
Executive Function	8	17.62	8.00	0.80	6-8	7.00	8.00	1.41	4-8	7.44	8.00	0.73	6-8
Language	18	6.90	18.00	1.70	15-18	16.90	17.50	1.45	14-18	17.00	18.00	1.66	13-18
Cross sectional		**Baseline (n=55)**				**4 months (n=43)**				**8 months (n= 39)**			
Memory	13	10.95	12.00	2.55	1-13	11.26	12.00	1.89	2-13	12.21	12.00	0.83	9-13
Attention	21	14.45	15.00	4.37	3-21	18.00	18.00	2.62	9-21	18.74	19.00	2.01	14-21
Visual Spatial	6	4.36	5.00	1.89	0-6	5.67	6.00	0.87	2-6	5.79	6.00	0.47	4-6
Executive Function	8	5.34	7.00	2.97	0-8	7.07	8.00	2.03	0-8	7.49	8.00	1.43	0-8
Language	18	14.18	16.00	4.09	3-16	17.14	18.00	1.36	13-18	16.59	17.00	1.55	12-18

Note: Minimum possible score for all cognitive domains was zero

5.3 Main Analysis

5.3.1 Inferential Statistics

By using inferential statistics, the study examined the differences between the cognitive-linguistic abilities of the groups and within the participants at the different time periods. Inferential statistics were done on both the CLQT and the interview schedule. Even though the interview schedule brought a qualitative flavor to the design, it was able to provide quatitive information from the closed ended questions when responses were tallied up and raw scores obtained. The study also investigated whether gender, age, education and CD4 counts influenced the cognitive-linguistic abilities of the participants.

AIM 1: To determine whether there is a significant difference in cognitive-linguistic abilities between the participants in the experimental, comparison and cross-sectional groups on the Cognitive Lingusitic Quick Test and the interview schedule.

A Kruskal-Wallis (K-W) one-way analysis of variance was run to determine whether a difference in cognitive-linguistic ability existed between the three groups at baseline, four months and eight months. A significant difference is said to occur if $p<0.05$. This test was also corrected for tied ranks. Follow-up post hoc tests were conducted to evaluate pairwise differences among the three groups at the three testing times (Green and Salkind, 2008)

Cognitive Linguistic Quick Test.

At baseline.

Results of analysis revealed significant differences between particpants in the groups performance for all the cognitive domains except for attention. The sigificant findings were as follows: Memory $\chi^2(2, N=132)=8.16$, $p=0.02$; Executive functions $\chi^2(2, N=132)=13.55$, $p=0.001$; Language $\chi^2(2, N=132)=15.24$, $p=0.0005$; Visual spatial $\chi^2(2, N=132)=8.40$, $p=0.02$. Based on these findings the researcher rejected the null hypothesis for all the cogntive domains domains except attention

Using pairwise comparison post testing analysis between the cross sectional and experimental groups - no significant differences for all five cognitive domains were observed.

Post testing analysis using pairwise comparisons showed that between the cross sectional and comparison groups significant difference were noted for all the domains except attention. The significant findings were as follows: Memory $\chi^2(1, N=77)=4.38$, $p=0.04$; Executive functions $\chi^2(1, N=77)=12.32$, $p=0.0004$; Language $\chi^2(1, N=77)=13.69$, $p=0.0002$; Visual spatial $\chi^2(1, N=77)=7.28$, $p=0.007$.

Post testing analysis using pairwise comparisons showed that between the experimental and comparison groups significant difference were noted for memory $\chi^2(1, N=76)=7.20$, $p=0.007$, executive functions $\chi^2(1, N=76)=10.95$, $p=0.0009$ and visual spatial skills $\chi^2(1, N=76)=6.77$, $p=0.009$.

At four months.

Results of analysis revealed no significant differences between participants in the group performances on any of the five cognitive domains. Therefore the researcher failed to reject the null hypothesis.

Using pairwise comparison post testing analysis between the three pairs of groups revealed that there were no significant differences in performance for all five cognitive domains.

At eight months.

Results of analysis revealed no significant differences in group performance on any of the five cognitive domains. Therefore the researcher failed to reject the null hypothesis.

Using pairwise comparison post testing analysis between the three pairs of groups revealed that there were no significant differences in performance for all five cognitive domains.

To summarise the univariate analysis on the CLQT, using the Kruskal – Wallis test revealed that significant differences between the groups mainly occured at baseline. Post hoc testing using pairwise comparisons showed that this mainly occurred between the cross sectional and comparison groups; and the experimental and comparisons groups.

Interview Schedule (IS)

At baseline

Results of analysis revealed signifinant differences in group performance for all the cognitive domains except for memory. The sigificant findings were as follows: Attention $\chi^2(2, N=132)=25.87$, $p=0.0001$; Executive functions $\chi^2(2, N=132)=12.66$, $p=0.002$; Language $\chi^2(2, N=132)=14.87$, $p=0.0006$; Visual spatial $\chi^2(2, N=132)=10.29$, $p=0.005$. Therefore the null hypothesis was rejected for all cognitive domains except memory.

Post testing analysis using pairwise comparisons showed that significant difference were noted for all the domains except memory between the cross sectional and experimental groups. The significant findings were as follows: Attention $\chi^2(1, N=111)=23.32$, $p=0.0001$; Executive functions $\chi^2(1, N=111)=6.82$, $p=0.009$; Language $\chi^2(1, N=111)=11.97$, $p=0.0005$; Visual spatial $\chi^2(1, N=111)=8.36$, $p=0.004$.

Post testing analysis using pairwise comparisons also revealed significant difference that between the cross sectional and comparison groups for all the domains except memory. The significant findings were as follows: Attention $\chi^2(1, N=77)=10.59$, $p=0.001$; Executive functions $\chi^2(1, N=77)=9.32$, $p=0.002$; Language $\chi^2(1, N=77)=7.76$, $p=0.005$; Visual spatial $\chi^2(1, N=77)=4.98$, $p=0.03$.

Using post testing analysis between the experimental and comparison groups no significant differences for all five cognitive domains were observed.

At four months.

Results of analysis revealed a significant difference in group performance in only one cognitive domain - visual spatial abilities $\chi^2(2, N=108)=8.58$, $p=0.01$. Therefore the researcher failed to reject the null hypothesis except for the domain of visual spatial.

Post testing analysis using pairwise comparisons showed that between the cross sectional and experimental groups significant difference were only noted for memory $\chi^2(1, N=111)=8.44$, $p=0.003$.

Post testing analysis using pairwise comparisons showed that between the cross sectional and comparison groups; and the experimental and comparison groups there were no significant differences noted for all five cognitive domains.

At eight months

Results of analysis revealed a significant difference in group performance in only one cognitive domain - memorys $\chi^2(2, N=100)=6.31$, $p=0.04$. Therefore the researcher failed to reject the null hypothesis except for memory.

Post testing analysis using pairwise comparisons showed that between the three different pairs significant difference were only observed between cross sectional and experimental groups for the cognitive domains of memory $\chi^2(2, N=91)=4.86$, $p=0.03$ and language $\chi^2(2, N=89)=8.46$, $p=0.004$.

In summary, performance for the Interview schedule using the Kruskal-Wallis tests revealed significant differences in cogntive-linguistic abilities between the groups mainly occurred at baseline. Post hoc testing using pairwise comparisons revealed that cross sectional and comparison groups along with the cross sectioanl and experimental grouping exhibited the most significant differences at baseline and four months However at eight months only the cross sectional and experimental groups were noted to have exhibited the most significant differences.

AIM 2: To determine whether there was a significant difference in cognitive-linguistic abilities within the participants (time effect) for the experimental and comparison groups on the Cognitive Lingusitic Quick Test and the interview schedule.

One-way repeated measures analysis of variance (ANOVA) was used to analyse whether there was a significant difference in cognitive-linguistic abilities in the participants across the three testing time periods of baseline, four months and eight months in the experimental and comparison groups (Howell, 2008). This statistical analysis was used because the same group of participants were measured at different times, namely at baseline, four and eight months. To use the one-way repeated measures ANOVA (RM-ANOVA), the data needed to meet the assumptions of sphericity. Sphericity, a special case of circularity assumptions, checks whether the variance/covariance matrix of the observed data follows a particular pattern (Chajewski, 2012). This pattern is usually identified as one with equal variances in the diagonal and equal covariance in the off-diagonal elements (Hamer, Wood Johnson & Simpson, 2000). This was determined using the Greenhouse-Geisser Epsilon (G-G) and the Huynh-Feldt Epsilon (H-F) tests.

This study used the PROC GLM method in SAS® to test for sphericity by identifying orthogonal covariance elements. This procedure ran uncorrected RM-ANOVA F-tests which usually result in the inflation of Type I Errors (Chajewski, 2012). It then ran several corrections most notably the Greenhouse-Geisser and Huynh-Feldt epsilon corrections. These do not affect the computed *F*-statistic, but instead raise the critical *F* value needed to reject the null hypothesis (Hamer, Wood Johnson & Simpson, 2000). For this data these corresponding corrective coefficients were: Greenhouse-Geisser $\varepsilon = <.75$ and Huynh-Feldt $\varepsilon = >.75$ (Larsson, 2012). The conditions were not met therefore corrections were not affected.

Repeated post hoc analysis was also done using the paired t-test. This test was run to test the significance of difference between two related samples, i.e. the same participants at the three testing periods of baseline, four and eight months.

The bolded numbers in Tables 5.10; 5.11; 5.12; 5.13 indicate significance at $p<0.05$

Cognitive Linguistic Quick Test (CLQT)

Table 5.10 summarizes the participants' performances. Repeated measures analysis revealed significant differences in performance within the individuals in the experimental group across all domains except for language. For within participant comparison group significant differences were observed for all domains except memory. Based on these findings the null hypothesis was rejected for the experimental group and the comparison group

Table 5.10 Repeated Measures ANOVA for the Experimental and Comparison group on the CLQT

Group	Domains	Observed	n	Mean Square	df	F	P-value
Experimental	Memory	55	51	1046.71	2	6.27	**0.003**
	Error			166.73	100		
	Attention	55	51	12313.2	2	26.88	**<0.009**
	Error			458.16	100		
	Exec. Functions	55	51	319.26	2	31.9	**<0.0001**
	Error			10.01	100		
	Language	55	51	29.08	2	2.9	0.08
	Error			-6.19	100		
	Visual Spatial	55	51	2819.03	2	38	**<0.0001**
	Error			74.18	100		
Comparison	Memory	21	9	321.6	2	1.52	0.25
	Error			211	16		
	Attention	21	9	874.33	2	4.23	**0.03**
	Error			206.58	16		
	Exec. Functions	21	9	36.33	2	5.42	**0.02**
	Error			6.71	16		
	Language	21	9	13.4	2	2.9	**0.08**
	Error			4.65	16		
	Visual Spatial	21	9	382.93	2	8.15	**0.004**
	Error			47.01	16		

The paired sample t-test analysis (see Table 5.11) revealed that the largest mean differences were observed from baseline and eight months within the participants in the experimental group on the CLQT. The greatest improvement from baseline was from baseline to four months. The smallest significant differences were noted between four and eight months. This could be due to a plateau effect. These trends observed in performance were similar to the mean scores recorded for the severity ratings (see Table 5.10) in that the severity rating of either mild or moderate did not change at four or eight months, even though the mean scores changed over time.

Table 5. 11 Post hoc Paired t-test analysis of the Participants in the Experimental and Control groups on the CLQT

Group	Effect	n	Compare	Mean Difference	Standard Error	t-value
Experimental	Memory	51	2-1	6.07	2.88	**0.04**
			3-1	9.04	2.4	**0.004**
			3-2	3.98	2.2	0.07
	Attention	51	2-1	22.35	4.29	**<.0001**
			3-1	30.25	5.19	**<.0001**
			3-2	8.98	2.64	**0.001**
	Exec. Functions	51	2-1	4.1	0.64	**<.0001**
			3-1	4.69	0.8	**<.0001**
			3-2	0.82	0.34	**0.02**
	Language	51	2-1	1.52	0.53	**0.007**
			3-1	0.73	0.42	0.1
			3-2	-0.84	0.49	0.09
	Visual Spatial	51	2-1	10.4	1.72	**<.0001**
			3-1	14.63	2.1	**<.0001**
			3-2	5	1.13	**<.0001**

Control	Memory	9	2-1	3.7	7.7	0.64
			3-1	11.78	7.41	0.15
			3-2	7.67	3.65	0.07
	Attention	9	2-1	16.5	9.02	0.1
			3-1	19.67	7.08	**0.02**
			3-2	8.67	4.85	0.11
	Exec. Functions	9	2-1	2.1	1.17	0.12
			3-1	4	1.06	**0.006**
			3-2	1.67	1.3	0.23
	Language	9	2-1	1	-1.17	0.42
			3-1	2.44	0.91	**0.02**
			3-2	1.33	0.75	0.11
	Visual Spatial	9	2-1	8.1	2.01	0.03
			3-1	12.78	3.18	**0.01**
			3-2	4.11	3.48	0.27

Overall the within-participant group performances on the Cognitive Linguistic Quick Test were significantly better for individuals in the experimental group than for those in the comparison group.

Interview Schedule (IS)

The univariate analysis presented in Table 5.12 revealed that the assumption(s) of sphericity were met for both the experimental and control groups. Since these assumptions were met, the parametric statistics of repeated measure analysis were used.

Repeated measures analysis, as presented in Table 5.12 revealed that significant differences in performance were observed within the individuals in all the cognitive-linguistic abilities except for memory in the experimental group across all three time periods. Conversely, a significant difference within participant performance was observed only for the domain of attention in the comparison group. Based on these findings the null hypothesis was rejected for the experimental group and accepted for the comparison group. This implies that individuals within the experimental group were experiencing greater effect changes over time - that is more improvement over time than the comparison group.

Table 5. 12 Repeated Measures ANOVA analysis for the Experimental and Comparison Groups on the IS

Group	Domains	n	Mean Square	df	F-value	P-value
Experimental	Memory	51	7.3	2	2.23	0.11
	Error		3.28	100		
	Attention	51	238.84	2	23.91	**<0.0001**
	Error		9.98	100		
	Exec. Functions	51	21.85	2	10.59	**<0.0001**
	Error		0.88	100		
	Language	51	85.77	2	14.69	**<0.0001**
	Error		5.88	100		
	Visual Spatial	51	9.3	2	7.54	**0.0009**
	Error		1.23	100		
Comparison	Memory	9	5.44	2	1.6	0.23
	Error		3.4	16		
	Attention	9	19.7	2	5.51	**0.02**
	Error		3.59	16		
	Exec. Functions	9	0.93	2	1.05	9.37
	Error		0.88	16		
	Language	9	85.77	2	1.28	0.3
	Error		0.9	16		
	Visual Spatial	9	1.04	2	1.79	0.2
	Error		0.58	16		

The paired t-test analysis (see Table 5.13) revealed that there were more significant differences in cognitive-linguistic abilities over time within individuals in the experimental group as compared to the comparison group. The largest mean difference was noted from baseline to eight months. The greatest improvement from baseline was observed from baseline to four months for most of the cognitive domains. These domains included attention, executive functions and language for the experimental group, and executive functions for the comparison group. The smallest significant differences were observed from four to eight months between participants in the experimental group. This could have been due to the plateau effect in abilities – improvement was starting to slow down and plateau

Table 5. 13 Post hoc Paired t-test analysis of the Participants in the Experimental and Control Groups on the IS

Group	Effect	n	Compare	Mean Difference	Standard Error	p-value
Experimental	Memory	51	2-1	0.6	0.4	0.14
			3-1	0.73	0.42	0.09
			3-2	0.18	0.17	0.32
	Attention	51	2-1	2.45	0.64	**0.0003**
			3-1	4.27	0.68	**<.0001**
			3-2	1.55	0.52	**0.004**
	Exec. Functions	51	2-1	1.09	0.53	**0.003**
			3-1	1.2	0.33	**0.0007**
			3-2	0.14	0.1	0.18
	Language	51	2-1	1.76	0.55	**0.002**
			3-1	2.49	0.54	**0.0001**
			3-2	0.61	0.21	**0.005**
	Visual Spatial	51	2-1	0.21	0.23	0.23
			3-1	0.82	0.18	0.18
			3-2	0.61	0.22	0.22
Control	Memory	9	2-1	1.4	0.91	0.16
			3-1	0.78	0.43	0.11
			3-2	0.78	1.04	0.48
	Attention	9	2-1	2	0.92	0.06

		3-1	2.44	1.33	0.06
		3-2	-0.22	0.78	0.78
Exec. Functions	9	2-1	0.4	0.5	0.44
		3-1	0.56	0.5	**0.03**
		3-2	0	0.24	1
Language	9	2-1	0.1	0.41	0.81
		3-1	0.67	0.41	0.41
		3-2	0.56	0.47	0.28
Visual Spatial	9	2-1	0.4	0.4	0.34
		3-1	0.67	0.33	0.08
		3-2	0.22	0.28	0.45

In summary, the experimental group showed more significant improvements in performing their activities of daily living based upon the analysis of their cognitive-linguistic skills.

AIM 3: To determine the effect of age, gender, education and CD4 count on cognitive-linguistic functioning in both the experimental and comparison groups at baseline, four months and eight months on the Cognitive Linguistic Quick Test and the interview schedule.

We extended the previous analysis in aim two to control for covariates by doing repeated measures analysis of covariates (ANCOVA). The three covariates structure models of Compound symmetry (CS), Huynh-Feldt (H-F) and Auto-regressive (1)(AR-1) were used. The three goodness of fit statistics used included the Akaike's information criteria (AIC), corrected Akaike's information criteria (AICC) and Bayesian information criteria (BIC). This analysis tested the assumption that the best fitting model would be chosen based on smaller AIC, AICC and BIC values and the residual distribution would be normally distributed with a mean of zero and a standard deviation between -1 and +1 (refer to Appendix IX for the studentized residual plots).

The ANCOVA analysis was run using Mixed Procedure in SAS®. This procedure was used for a number of reasons. Firstly, this procedure does not require balanced data across the different testing times. This enables more flexibility and allows for more power when handling unbalanced data (e.g., unequal sample size, inconsistent time interval, and missing data). This is important in longitudinal studies in which the problems of participant dropout and other forms of missing measurements within individuals are often encountered (Shek & Ma, 2011). Secondly, it allows researchers to study both between group and within

group differences. Third, this mixed procedure analyses estimates the changes in parameters with greater precision when the number of time waves is increased. This improves the reliability of the change parameters by reducing standard errors of the within-subject changes in the parameters estimates (Willett, Singer & Martin 1998). The independent variables were age, CD4 counts, education and gender. The dependant variables were time of testing and group. Covariances included all five cognitive domains – attention, memory, executive functions, language and visual spatial skills. The results of the ANCOVA were discussed by keeping all other independent variables constant and are discussed for both the CLQT and IS.

Cognitive Linguistic Quick Test (CLQT)

According to the results (see Table 5.14), the assumption stating that the residuals were normally distributed with a constant variance (also see studentized residuals in Appendix IX) was met. Therefore we continued to interpret the results using the repeated measures ANCOVA analysis.

Table 5.14 Information Criterion among the three Covariance Structure Models on the CLQT

Covariances	Covariance structure	AICC	AIC	BIC
Attention	Compound symmetry (df =3)	1654.8	1654.6	1663.3
	Huynh-Feldt (df=7)	**1636.9**	**1636**	**1653.4**
	Auto Regressive (1) (df=3)	1661.8	1661.6	1670.3
Memory	Compound symmetry (df =3)	1461.7	1461.4	1470.1
	Huynh-Feldt (df=7)	1468.3	1467.3	1484.7
	Auto Regressive (1) (df=3)	**1455.6**	**1447.3**	**1464**
Exec. Functions	Compound symmetry (df =3)	1036.1	1035.8	1044.5
	Huynh-Feldt (df=7)	**1035.4**	**1034.5**	**1051.9**
	Auto Regressive (1) (df=3)	1047.3	1047	1055.7
Language	Compound symmetry (df =3)	879.2	878.9	887.6
	Huynh-Feldt (df=7)	882	881.1	898.5
	Auto Regressive (1) (df=3)	**878.8**	**878.6**	**887.3**
Visual Spatial	Compound symmetry (df =3)	1364.4	1364.1	1372.8
	Huynh-Feldt (df=7)	**1354.6**	**1353.7**	**1371.1**
	Auto Regressive (1) (df=3)	1378.9	1378.7	1387.4

Note: Numbers bolded indicate the best fitting model.

The results below were discussed according to how the variables influenced each domain as presented in Table 5.14.

Attention:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7

parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Huynh-Feldt was the best model in fitting the data.

Age was found to have a significant effect on attention because as a person got older in years attention scores were lowered (β = 0.45, SE = 0.11, p <0.01) all other variables were kept constant. Gender was also found to have a significant main effect on attention when all other variables were kept constant. Females overall had higher scores than males (β = 5.41, SE = 1.85, p <0.01). Lastly CD4 count had a significant main effect on attention when all other variables were kept constant. As the CD4 count increased by one, attention scores improved (β = 0.03, SE = 0.01, p <.0001). Based on these results the null hypothesis was rejected for all independent variables except education.

Memory

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Auto regressive (1) model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Auto regressive (1) was the best model in fitting the data.

The only variable found to have a significant main effect on memory was education when all other variables were kept constant. As education levels increased by one year of study, memory mean scores got higher (β = 1.64, SE = 0.64, p <.01). Based on this finding the null hypothesis failed to be rejected for all independent variables except education.

Executive functions:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, $\Delta df = 4$, $p < .0001$). This suggested that Huynh-Feldt was the best model in fitting the data.

Education also had a significant main effect on memory when all other variables were kept constant. As education levels increased by one year of study, memory mean scores got higher ($\beta = 0.86$, $SE = 0.17$, $p < .01$). The researcher therefore failed to reject the null hypothesis for all independent variables except education.

Language:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Auto regressive (1) model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, $\Delta df = 4$, $p < .0001$). This suggested that Auto regressive (1) was the best model in fitting the data.

The only variable to exhibit significant a main effect on language was education when all other variables were kept constant. As education levels increased by one year of study, language mean scores got higher ($\beta = 0.38$, $SE = 0.1$, $p < .01$). The researcher therefore failed to reject the null hypothesis for all independent variables except education.

Visual Spatial

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, $\Delta df = 4$, $p < .0001$). This suggested that Huynh-Feldt was the best model in fitting the data.

Age was found to have a significant main effect on visual spatial skills because as a person got older in years visual spatial scores were lowered ($\beta = -0.25$, $SE = 0.09$, $p < .01$) all other variables were kept constant. Education was also found to have a main significant effect on visual spatial skills when all other variables were kept constant. As education levels increased by one year of study, visual spatial mean scores got higher ($\beta = 2.14$, $SE = 0.18$, $p < .0001$). Since age and education had significant main effects on visual spatial skills the null hypothesis was rejected for these variables only.

Interview Schedule

The assumption stating that the residuals were normally distributed with a variance of 1 (also see studentized residuals in Appendix IX) was met. Therefore we continued to interpret the results using the repeated measures ANCOVA analysis.

Table 5.15 Information Criterion among the three Covariance Structure Models on the IS

Covariances	Covariance structure	AICC	AIC	BIC
Attention	Compound symmetry (df =3)	955.2	954.9	963.6
	Huynh-Feldt (df=7)	**928.1**	**927.1**	**944.5**
	Auto Regressive (1) (df=3)	944.5	966	974.7
Memory	Compound symmetry (df =3)	833.9	833.7	842.4
	Huynh-Feldt (df=7)	**819**	**818.1**	**835.5**
	Auto Regressive (1) (df=3)	827.6	827.4	836.1
Exec Functions	Compound symmetry (df =3)	704	703.8	712.5
	Huynh-Feldt (df=7)	704.1	703.2	720.6
	Auto Regressive (1) (df=3)	**695**	**694.7**	**703.4**
Language	Compound symmetry (df =3)	808	807.8	816.5
	Huynh-Feldt (df=7)	**733.1**	**732.2**	**749.6**
	Auto Regressive (1) (df=3)	811.7	749.6	820
Visual Spatial	Compound symmetry (df =3)	578.4	578.1	586.8
	Huynh-Feldt (df=7)	**563.1**	**562.2**	**579.6**
	Auto Regressive (1) (df=3)	585.8	585.5	594.2

Note: Numbers bolded indicate the best fitting model.

The results below were discussed according to how the variables influenced each domain as presented on Table 5.15.

Attention

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e 7

parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Huynh-Feldt was the best model in fitting the data.

Univariate analysis showed that Age, CD4 counts, education and gender did not have a significant main effect on attention. Therefore the null hypothesis failed to be rejected.

Memory:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e 7 parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Huynh-Feldt was the best model in fitting the data.

Age had a significant main effect on memory abilities when all other variables were kept constant. As age increased by one year, attention scores lowered (β = -0.13, SE = 0.03, p <0.0001). The researcher therefore failed to reject the null hypothesis for all independent variables except age.

Executive functions:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Auto regressive (1) model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom

(i.e. 7 parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Auto regressive (1) was the best model in fitting the data.

Univariate analysis showed that Age, CD4 counts, education and gender did not have a significant effect on executive functions. Therefore the null hypothesis failed to be rejected.

Language:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, Δdf = 4, p <.0001). This suggested that Huynh-Feldt was the best model in fitting the data.

Age had a significant main effect on language abilities when all other variables were kept constant. As age increased by one year, language scores lowered (β = -0.03, SE = 0.01, p = 0.02). The researcher therefore failed to reject the null hypothesis for all independent variables except age.

Visual spatial:

The smallest values in the three goodness of fit criterion (Akaike's information criteria [AIC], corrected Akaike's information criteria [AICC] and Bayesian information criteria [BIC]) were found in the Huynh-Feldt model. These differences were significant when compared to the results of a chi-square distribution with degrees of freedom (i.e. 7 parameters – 3 parameters, $\Delta df = 4$, $p < .0001$). This suggested that Huynh-Feldt was the best model in fitting the data.

Age had a significant main effect on visual spatial abilities when all other variables were kept constant. As age increased by one year, visual spatial scores lowered ($\beta = -0.05$, SE = 0.01, $p = 0.001$). The researcher therefore failed to reject the null hypothesis for all independent variables except age.

In summary, ANCOVA analysis revealed that the assumption of the residuals being normally distributed was met with a variance of 1. The ANCOVA results showed that the most common best fit model for the domains for both the CLQT and the interview schedule was the Huynh-Feldt model followed by the auto-regressive model (1). The variables that significantly influenced cognitive-linguistic abilities on the CLQT were observed to be education and to a lesser extent age (attention) and CD4 count (language). The ANCOVA results for the interview schedule showed the variable that most influenced the participants' cognitive-linguistic abilities to perform activities of daily living was age (memory, language and visual spatial skills).

5.4 Content Analysis

The data collected from the semi-structured interview schedule was analysed using content analysis. This was done to provide more discussion and interpretation of the participants' responses and compliment the results of the Cognitive Linguistic Quick Test.

AIM 4: To investigate the cognitive-linguistic functioning that affected the ability to perform activities of daily living in the experimental, cross-sectional and comparison groups.

To attend to this aim the open-ended questions were analysed using quantitative thematic content analysis. This analysis provided the participants' personal experiences and perceptions to compliment the statistical findings from the CLQT and the Interview schedule. Analysis revealed four categories. These included attention, visual, expressive and receptive language. The responses for the category of attention were further divided into the sub-themes of pain, emotion and other. As previously mentioned in the literature review, the ability to attend to tasks of daily living can be affected by internal and external distracters. Internal distracters are factors that arise from within the individual that affect how an individual attends to activities of daily living (ADLs). External distracters would include factors outside of the individual in their environment that would affect how they can attend to a task. For participants in all three groups internal distracters greatly impacted on their ability to attend to ADLs.

The other pre-determined categories of visual, expressive and receptive language abilities were also further divided into themes. Visual abilities were divided into the themes of pain, discharge and "other". Expressive and receptive language had one sub-category each

that was further divided into different clusters. The categories of expressive and receptive language included the themes of speech and hearing respectively. See Tables 5.17; 5.18 and 5.19 for the frequencies of emergent themes at baseline, four and eight months.

Baseline

Frequency statistics using percentages for all three groups were calculated for the participants' responses on the interview schedule (refer to Table 5.16)

Table 5. 16 Frequencies of Emergent Themes by the Three Groups at Baseline

Cognitive –linguistic abilities			Experimental		Comparison		Cross sectional	
	Themes	**Sub - themes**	**N**	**n(%age)**	**N**	**n(%age)**	**N**	**n(%age)**
Attention	Pain	Headaches	30	11(37)	11	4(37)	37	15(40)
		Feet and Hands		5(17)		2(18)		7(20)
		Whole body		1(3)		1(9)		4(11)
		Neck		2(6)		0		
		Chest		4(13)		1(9)		2(5)
		Abdomen		1(3)		0		4(11)
		other		6(21)		3(27)		5(13)
	Emotion	Stress	12	2(16.5)	3	0	14	4(29)
		Sadness and Depression		5(42)		3(100)		8(57)
		Anger		3(25)		0		2(14)
		Fear		2(16.5)				
	Other	Dizziness	11	3(27)	4	0	8	2(25)
		Blackouts		0		0		1(12.5)
		Fatigue		8(73)		4(100)		5(62.5)
Visual	Pain		5	1(20)	0		6	3(50)
	Discharge			1(20)				0
	other			3(60)				3(50)
Express.lang			2	2	0	0		0
	Speech	Hoarse	7	7(100)		0	2	1(50)
		Intensity		0		0		
		Rate		0		0		1(50)

Rec. Lang			0	0	0	0		
	Hearing	Hearing probs	5	2(40)	0	0	3	2(67)
		Discharge		2(40)		0		
		Ringing		1(20)		0		1(33%)

Note: The responses indicated by category may not be equal to the total number of participants recruited at each time period because respondents may have reported no cognitive – linguistic problems, and those who did respond may have reported more than one category.

Participant responses shown on Table 5.16 revealed that at baseline the majority of the responses from all three groups cited attention as the domain most affecting their ability to perform activities of daily living (ADLs). Pain, emotions and "other" as an internal distracters were the main reasons or subthemes that emerged as to why they could not attend to ADLs. Most of the complaints about pain from the participants in all groups included headaches, hand and foot soreness and numbness attributable to peripheral neuropathy, and chest pains which were attributed to a pulmonary infection. In the "other" sub-theme of pain respondents complained about a painful rash over the whole body or certain parts of the body.

Under the themes of emotions different sub themes emerged – sadness, fear, anger and stress were cited as reasons for not being able to attend. Sadness obtained the highest numbers of responses in the theme of emotions from all the groups - experimental (5 out of the 10), comparison (3 out of 3) and cross sectional (8 out of 14). Respondents stated that they "[I felt] sadness after my diagnosis" and "I get sad when I think of my status." Participants who reported anger (three out of 10) and stress (two out of 10) as the main reason why they could not attend to task said:

… [I] get angry when I think of how I contracted HIV,"

… [I got] angry when I found out I was positive…

… [I got] angry because of my husband's death… I feel stressed with the children.

Fear was also cited as a sub theme of emotion two out of ten responses from the experimental group indicated that were fearful. A respondent stated that "[I] fear when I think of my low CD4 count. Another said "[I'm] worried about my children."

In the “other” category of attention, the majority of respondents in all three groups complained of fatigue as the main reason for them not being able to attend to ADLs and dizziness. From the experimental there were eight out of 11 responses; comparison all the respondents; and five out of eight responses from the cross sectional. Respondents stated that they felt tired and found it difficult to concentrate or even have the energy to start or complete an activity, The response were “[I] feel tired in the morning,” and “ [I] want to sleep a lot.” Responses to the sub – theme of dizziness could have been indicative of the effects of HI virus in the brain since the participants had not yet started to take HAART.

There were not many participants that indicated they had visual spatial problems. The few respondents in both the experimental (five) and cross sectional (six) groups indicated having visual problems that were affecting their ability to perform ADLs. The sub themes that emerged included painful eyes, discharge and other. From the experimental group one out of five responses and three out of six responses from the cross sectional group indicated that they had painful eyes. The ‘other’ category had the most responses from the experimental (three out of five) and cross sectional (three out of three) groups and they included comments like eye problems after meningitis, “can’t see when it is dark”, and “shingles in the left eye”.

Regarding the category of expressive language, speech emerged as the main theme with sub themes of hoarse, intensity and rate. All seven respondents in the experimental group indicated that their vocal quality was hoarse. In the cross sectional group one participant stated they were speaking much slower and another reporting that their spoke with a “low” voice. Receptively, two out of five responses from the experimental and two out of three cross sectional groups reported experiencing hearing problems that is the right or left

ear not hearing properly. The other sub –themes that respondents commented on included, yellowish discharge and ringing noise in their ears.

Surprisingly, no visual, expressive or receptive language difficulties were reported by the participants in the comparison group

Four months

Frequency statistics using percentages for all three groups were calculated for the participants' responses on the interview schedule (refer to Table 5.17)

Table 5. 17 Frequencies of Emergent Themes by the Three Groups at Four months

			Experimental		Comparison		Cross-sectional	
Categories	**Themes**	**Sub themes**	**N**	**n(%age)**	**N**	**n(%age)**	**N**	**n(%age)**
Attention	Pain	Headaches	4	1(25)	1	0	6	2(33)
		Feet and Hands		1(25)		0		
		Whole body		0		1(100)		2(33)
		Neck		0		0		
		Chest		0		0		1(16.5)
		Abdomen		0		0		
		other		2(50)		0		1(16.5)
	Emotion	Stress		0	1	0		
		Sadness and Depression		0		1(100)		
		Anger		0		0		
	Other	Dizziness	3	1(33)	2	0	2	0
		Blackouts		0		1(50)		0
		Fatigue		2(67)		1(50)		2(100)
Visual	Pain		1	0	1	0	3	2(67)
	Discharge			0		0		0
	other			1(100)		1(100)		1(33)
Express.lang			1	1(100)	0	0	0	0
	Speech	Hoarse	2	0	0		1	0
		Intensity		1(50)				1(100)
		Rate		1(50)				0

Rec. Lang			1	1(100)	0	0	0	0
	Hearing	Hearing probs	2	2(100)	0		1	0
		Discharge		0				1(100)
		Ringing		0				0

Note: The responses indicated by category may not be equal to the total number of participants recruited at each time period because respondents may have reported no cognitive – linguistic problems, and those who did respond may have reported more than one category.

The responses presented in Table 5.17 revealed a similar trend to the baseline results in that more participants complained of attentive internal distraction problems. However, the numbers of responses were less than at baseline especially for the experimental and comparison groups.

From the category of attention, the theme of pain received more responses in the cross sectional group than the experimental or comparison. A respondent stated that … [I am experiencing] headaches more after [I] started taking ARVs …pain in right hand palm.

Responses from the cross sectional group (four out six) complained of either headaches or all over body aches. Only two individuals complained of pain and one in the comparison group. However, it was observed that in the 'other' category that the sub – theme fatigue was still a complaint of the participant (s) in all three groups. One participant in the comparison reported they had experienced a black out. Another respondent said "… [I] get dizzy when I take my medication."

Visual and language problems also reflected a decrease in responses as compared to baseline. Regarding the theme of visual pain two out of three responses in the cross sectional group indicated they their eyes were painful. One participant in all three groups indicated that they were having visual spatial problems in the other category. These were among same participants who had reported in the other category at baseline.

The language categories yielded very few responses. One response reported experiencing difficulties expressing their thoughts and ideas in the experimental group. In the theme of speech one respondent in both the experimental and cross sectional group reported that they problems with the loudness of their voice. They commented that their voices were

soft. Only one respondent reported speech rate as a problem and that was in the experimental group.

Eight months

Frequency statistics using percentages for all three groups were calculated for the participants' responses on the interview schedule (refer to Table 5.18)

Table 5.18 Frequencies of Emergent Themes by the Three Groups at Eight months

Categories	Sub-Cat		Experimental N	Experimental n(%age)	Comparison N	Comparison n(%age)	Cross sectional N	Cross sectional n(%age)
Attention	Pain	Headaches	0	0	14	5(36)	3	0
		Feet and Hands		0		5(36)		0
		Whole body		0		0		2(67)
		Neck		0		1(7)		0
		Chest		0		2(14)		0
		Abdomen		0		0		0
		other		0		1(7)		1(33)
	Emotion	Stress	0	0	2	2	0	0
		Sadness and Depression		0		0		0
		Anger		0		0		0
	Other	Dizziness	0	0	0	0	2	0
		Blackouts		0		0		0
		Fatigue		0		0		2(100)
Visual	Pain		0	0	1	0	2	1(50)
	Discharge			0		0		1(50)
	other			0		1		0
Express.lang	Speech	Hoarse	0	0	0	0	0	0
		Intensity		0		0		0
		Rate		0		0		0

Rec. Lang	Hearing probs	0	0	0	0	1	1(100)
	Discharge		0		0		0
	Ringing		0		0		0

Note: The responses indicated by category may not be equal to the total number of participants recruited at each time period because respondents may have reported no cognitive – linguistic problems, and those who did respond may have reported more than one category.

The reported results listed in Table 5.18 showed that the comparison group reported more cognitive –linguistic problems especially in the domain of attention. Most of the responses (14) from the comparison group complained that attentive internal distractions affected their abilities to focus on or complete activities of daily living. The theme of pain from headaches and hands and feet were cited as being especially worrying among the respondents. In contrast, the experimental and cross-sectional groups reported very few to no cognitive-linguistic difficulties. Problems reported especially from the cross-sectional group included two responses from the visual spatial theme and another for the theme of hearing problems. The decrease in the cognitive –linguistic complaints could have indicated that participants were feeling better due to the increased CD4 counts as presented in Table 4.6 (methodology chapter).

Overall, the ability to perform activities of daily living also appeared to have improved across the three time periods. There were more reported cognitive – linguistic problems at baseline that decreased with each successive testing. When the participants were asked how their cognitive-linguistic abilities were impacting on their activities and participation in their environments, the category of attention with the sub themes of pain, emotions, fatigue and dizziness received the most responses especially at baseline and four months. The comparison group responses were higher at baseline and eight months. The results of inferential testing revealed that as greatest main effect usually occurred from baseline to eight month on the cognitive linguistic abilities. However, the descriptive results on the severity ratings did not concur with the reported cognitive linguistic abilities. For example an individual who was reported to have severe memory and executive problems clinically was able to use public transportation and make their way to the clinic.

Chapter 6: Discussion

6.1 Introduction

The results of this study supported the main hypothesis that HAART improves the cognitive-linguistic abilities of adults living with HIV and AIDS over time. The main findings of this study revealed that significant differences between the groups mainly occured at baseline. Post hoc testing using pairwise comparisons showed that this mainly occurred between the cross sectional and comparison groups; and the experimental and comparisons groups on the Cognitive Linguistic Quick Test. Performance on the Interview schedule revealed significant differences in cogntive-linguistic abilities between the groups mainly occurred at baseline. Post hoc testing using pairwise comparisons revealed that cross sectional and comparison groups along with the cross sectioanl and experimental grouping exhibited the most significant differences at baseline and four months. However at eight months only the cross sectional and experimental groups were noted to have exhibited the most significant differences.

Significant differences in performance within the individuals in the experimental group were observed for all domains except language; and within the comparison group, significant differences were observed for all domains except memory on the CLQT. Post testing revealed the largest mean differences between baseline and four months and the smallest significant differences were noted between four and eight months. This could have been due to a plateau effect. On the Interview schedule significant differences in performance were observed in all the cognitive-linguistic abilities except for memory within individuals in the experimental group. Conversely, a significant difference within participant performance was observed only for the domain of attention in the comparison group. This implied that individuals within the experimental group were experiencing greater effect changes

over time - that is more improvement over time than the comparison group. The paired t-test analysis (see Table 5.16) revealed that there were more significant differences cognitive-linguistic abilities over time within individuals in the experimental group as compared to the comparison group. The largest mean differences were observed from baseline to four months for most of the cognitive domains. These domains included attention, executive functions and language for the experimental group, and executive functions for the comparison group. The smallest significant differences were observed from four to eight months between participants in the experimental group. This could have been due to the plateau effect in abilities –improvement was starting to slow down and plateau. Overall the within group performances on the Cognitive Linguistic Quick Test were significantly better for individuals in the experimental group than for those in the comparison group.

The ANCOVA results showed that the variables that significantly influenced cognitive-linguistic abilities on the CLQT were observed to be education and to a lesser extent age and CD4 count. The ANCOVA results for the interview schedule showed the variable that most influenced the participants' cognitive-linguistic abilities to perform activities of daily living was age. Qualitative inquiry using content analysis showed that participants in all three groups cited attention, followed by visual and language problems as hindering their abilities to perform activities of daily living. Below is a discussion of the results and the demographic information of the participants as well as the challenges encountered conducting this research.

6.2 Descriptive results

Results of the descriptive analysis revealed that as the mean scores improved over time, the standard deviations went down for participants in the experimental, comparison and cross-sectional

groups on both instruments. The findings for the experimental group and cross-sectional group were expected across time. Conversely, the results for the comparison group were not expected. It was assumed that the mean scores for the comparison group would drop instead of increasing. The performance of the comparison group could have been due to the higher CD4 counts of the participants at the three testing periods and/or the practice effect. However, the descriptive analysis of the cross-sectional group reflects the same trend in performance of the experimental group even though different participants were used across all three time periods. Therefore, based on the cross-sectional performance, the practice effect argument for improvement in the comparison group is somewhat weakened.

The severity ratings of the participants in all three groups showed that even though the mean scores increased over time the cognitive-linguistic deficits still persisted among the participants, particularly in the mild range. These results were consistent with those found by Heaton et al. (2010). Heaton et al. (2010), in their cross-sectional study with 1555 HIV-infected adults, reported that more than half of their total sample had neurocognitive impairments. They found that although HAART had a positive impact on CNS manifestations including HIV-associated neurocognitive disorders, 44% of their participants continued to exhibit milder forms of HAND. They concluded that their patients improved because HAART probably benefitted the brain via multiple mechanisms, including immune recovery and viral suppression – both systemically and in the CNS. However, their participants had higher education levels (12.5 years) and CD4 counts (262 cells/mm^3 – 603 cells/mm^3) than those in the current study.

Another explanation for persistent cognitive-linguistic deficits even after HAART initiation could be due to the continued display of on-going brain volume decreases. Cardenas et al. (2009) purported that decreased brain volume after HAART initiation reflected continued viral infection in

the brain despite effective viral suppression in the periphery. This was due to the limited permeability of the blood brain barrier to most HAART; they hypothesized that the brain could serve as a reservoir for inactive infected macrophages

6.3 Differences between group performances

The results of the one way analysis of variance revealed that were significant differences between the experimental, comparison and cross sectional at baseline only. Most of significant differences occurred between the comparison - cross sectional (attention, visual spatial, executive functions, and language) and comparison – experimental groups on the CLQT. Whilst on the IS most of the significant differences occurred between the cross sectional -comparison groups and cross sectional-experimental groups. The results of this study were partially similar to the Sacktor et al. (2009) study. The results of this were partially similar in that this study was only able to show a significant between group differences at baseline only and Sacktor et al. showed significant differences between groups at all testing times. Sacktor et al. (2009) in their Ugandan study reported that there was a significant difference between HIV infected participants who had initiated HAART and those who had not. They followed and tested the participants in both groups at baseline, three and six months. They assessed both neurocognition and functional performance. Sacktor et al. also observed these differences on the functional performance scale (Karnofsky Performance Scale) as well. The differences between group performances for this study versus those of Sacktor et al. could have been due to the specific drugs used in the HAART cocktail or the clade type. Research (Baldeweg et al. 1998; Cysique, et al. 2004; Letendre et al. 2006; Letendre et al. 2008) has shown that antiretrovirals have different CNS penetration. Both Cohen et al. and Sacktor et al. did not

specify the specific drugs used in the HAART cocktail of their participants. Lastly, the clade type documented in Uganda is different from that in South Africa. Clades A and B are predominately in Uganda and C in South Africa.

6.4 Within group differences or improvement.

The results of this current study supported the hypothesis that HAART improves the cognitive-linguistic abilities. The participants in both groups basically demonstrated improvement across the three testing times. Significant differences were observed on the CLQT for the experimental were seen on all cognitive domains except language. Whereas, significant differences or improvements were seen on all cognitive domains except memory for the comparison group. The participants in the experimental group performed better than those in the comparison group on the CLQT. However, on the IS significant differences in performance within the experimental group were observed for all domains except language. Conversely significant difference or improvement was observed in the domain of attention only for the comparison group. These observations were made across all three testing times. The results observed by the experimental group in this study were similar to those of Cysique et al. (2009) and Letendre et al. (2007). Both of these studies were longitudinal and used HIV infected individuals (males and females) who were treatment naive at baseline. Letendre et al recruited 15 participants and assessed their neurocognitive abilities at baseline and 12 weeks after HAART initiation. Cysique et al used 37 participants who they tested at baseline, 24, 36 and 48 weeks after HAART initiation. These studies were different from this study in that they did not have a comparison and or control. In addition they did not assess functional performance. However findings from both

studies showed that there were significant differences/improvements in their participants once they initiated HAART as was shown in this study.

The improvement observed in the experimental group could have been due to the neuro-protective nature of ARVs in that they suppress HIV replication and improve the immune function by boosting the number of T-cells. Kipnis, Derecki, Yang and Scrable (2008) hypothesized that the immune system is intimately interwoven with brain function. Hence, immune malfunction may lead to cognitive impairment. According to these authors, neither systems (i.e. the CNS and immune system) can function optimally without the other; indeed, it is only because of their interactive functioning that the systems can coexist, and be of benefit to the individual. In addition, the ARVs in the 1a regimen that the majority of participants in this study were taking have been cited as having an intermediate (0.5) CNS penetration effect (Letendre, Woods, Ellis et al., 2006), implying that the ARVS in regimen 1a had a relatively good effect on cognitive-linguistic abilities. A further assumption could be made that the participants were also adhering to their HAART regimen and this facilitated the active suppression of the virus (Cysique, Vaida, Letendre, Vaida, Letendre et al., 2009).

It was expected that the experimental group would not only show improvement on the CLQT and but also on the the IS. These results of the experimental group were similar to the findings of Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al. (2009) even though the methodology was different. In Sacktor et al's study the other recruited group was HIV negative individuals as opposed to this study that recruited HIV positive individuals who elected not to initiate HAART. They recruited 102 HIV positive individuals and 25 HIV negative individuals. They used a functional assessment test, the Karnofsky Performance Scale, which was used at baseline, three months and six months after HAART initiation. Improvements were observed at three and six months in the

performance of functional everyday tasks. Functional abilities improved in HIV positive individuals from being severely impaired to the extent that individuals could not continue to work; to where at the end of six months they were able to perform everyday activities of daily living with independently. Their results possibly imply that HAART improved the participants' abilities to perform functional everyday activities.

However, it was puzzling that the comparison group showed improvement on the CLQT but not on the Interview Schedule. The improvement on the CLQT could be indicative of the slightly higher CD4 count of the comparison participants. Moreover, the results of the comparison group on the CLQT may have been different if the researcher had been able to recruit a "true control" versus a comparison group. However, due to constraints beyond the examiners control this was not possible as explained in the rationale. However, a lack of improvement demonstrated on the IS could have been indicative of an increase in viral load. Participants even though they presented with slightly higher CD4 counts at baseline, the counts were slowly decreasing over four and eight months because they had not initiated HAART. The participants may have been experiencing the effects of an increased viral load which were affecting their ability to perform activities of daily living.

Even though global impairments were observed in both the experimental and comparison groups, memory was more affected in the experimental than the comparison group. In this study participants in the experimental and comparison group exhibited memory impairments. According to Helm-Estabrooks (2001), "memory is not a single entity, but rather a complex process that enables us to attend to and register new information; to retain, process, and store (learn) this information" (p. 3) An aspect of memory, short-term or working memory, may be defined as a "system" for the temporary holding and manipulation of new or previously learnt information during the performance of cognitive task or activity. (Helm-Estabrooks, 2001; Panegyres, 2004). Several models have been

proposed to explain how working memory manipulates new or previously learnt information, and the most widely accepted is that of Baddeley's. Baddeley's model of working memory states that information is manipulated upon through the interaction of a central executive part, phonological loop and a visual spatial scratch pad (Baddeley, 2003, 2009). Problems in the central executive manifest as difficulties in organizing new materials and applying new strategies (Panegyres, 2004). Some researchers purport that these difficulties are indicative of cortical-subcortical circuitry damage (Ernst, Chang & Arnold, 2003; Kozoil & Budding, 2009). To further substantiate fronto-striatal system disruption, Ernst et al. (2003) found in their study of individuals with mild HIV brain disease that there was a positive correlation in glial markers in the frontal white matter and grey matter with working memory network activation. Their findings suggest that working memory abnormalities in HIV-positive individuals are driven by glial abnormalities in the white matter and basal ganglia. These findings lend support to the theory that cognitive-linguistic deficits exhibited by individuals who are HIV-positive rely on fronto-striatal circuitry and the neocortex (Cardenas et al., 2009; Melrose et al., 2008; Thompson, Dutton, Hayashi, Lu et al., 2006).

Post testing using the paired sample t-test revealed that the largest differences in performance were from baseline to four months for all cognitive domains for both groups. On the CLQT the greatest improvements from baseline performance were seen with attention, visual spatial and memory skills; the least was observed with language with the experimental group on the CLQT. The smallest significant differences were observed from four to eight months between participants in the experimental and comparison groups. Whilst on the IS the greatest improvement from baseline was observed from baseline to four months for most of the cognitive domains. These domains included attention, executive functions and language for the experimental group, and executive functions for the comparison group. The smallest significant differences were observed from four to eight months

between participants in the experimental group. This could have been due to the plateau effect in abilities. The improvement in cognitive – linguistic abilities was starting to slow down and plateau.

These results were similar in some part to Cysique, Vaida, Letendre, Vaida, Letendre et al. (2009) who reported that the greatest improvements were noted with those abilities that had the lowest baseline performance. However, they did not comment on which cognitive abilities they found this to be so. It was therefore difficult to adequately compare results fully. A study that exhibited partly dissimilar results to this study was conducted by Cohen et al. (2001). They showed that more improvement was noted at 18 months than 12 months of taking HAART. They found that of the four cognitive domains (psychomotor, memory, executive functions and language) tested, executive functions were the most impaired and language and memory the least impaired for all groups, but all domains improved significantly for those taking HAART. They did not assess functional performance. The only similarity in results in their study was language and memory being least affected and showing the least improvement. However results differ in terms of which domain had greatest improvement, in Cohen et al's study it was executive functions. In this study it was attention. The difference could be explained by the length of the study, gender tested and educational levels. Cohen et al's study was longer by 10 months; their participants were all women who had mean educational level of 12.5 years. The participants in this study were of mixed gender (even though more women were recruited) with an approximate mean level of 9.0 years. Furthermore, the fact that attention followed by visual spatial abilities and memory showed the greatest improvement from baseline could be indicative of synaptodendentric injury (Ellis et al., 2007). If attention is impaired then information processing is also impaired. The way we process information is determined by the speed of nerve impulses for one nerve to another. Synaptodendentric injury slows down and interrupts the speed of nerve electrical impulses thereby affecting attention and how we process information (Ellis et al., 2007).

Irrespective of similar and or dissimilar findings both findings support the theory that HIV-associated neurocognitive deficits (HAND) are underpinned by cortical and sub cortical neuronal circuitry. Woods et al. (2004) and Melrose et al. (2008) have suggested that attention and executive function impairments are consistent with the neuropathogenesis of HIV disease which predominantly affects cerebral white matter, basal ganglia, and the frontal neocortex. This has been supported by the neuro-imaging studies conducted by Ances et al. (2006), Berger et al.(2000), Ellis et al. (2007); Thompson, Dutton, Hayashi, Toga et al (2005); Thompson, Dutton, Hayashi, Lu et al. (2006) which were discussed in detail in the literature review (section 2.4.3).

It is not unusual for individuals living with HIV and AIDS to exhibit language abilities minimal language problems that fall within the mild to normal ranges before and after HAART initiation as found in this study. These results were supported by Bhat and Mathew (2008) who found in their cross sectional studies of eight HIV-positive individuals. The researchers showed that the participants in their study performed within normal limits on the Western Aphasia Battery (WAB). The WAB compromises mainly of "straight" linguistic processing tasks. Similar findings have also been reported in patients with sub-cortical damage such as Parkinson's and Huntington's Chorea where individuals exhibit normal language functioning on straight processing skills but exhibit difficulties on those language skills that rely heavily on higher-order thinking skills such as memory, executive functioning and attention such as phonemic or letter fluency (Marinus et al., 2003). Letter or phonemic fluency entails using new strategies to retrieve previously stored items in semantic memory and this involves both cortical and sub-cortical structures (Koziol & Budding, 2009). Furthermore, the language problems displayed by the participants in this study were indicative of impairments within short-term memory and long-term memory such as in answering questions pertaining to a short paragraph

presented to them and verbal fluency tasks, particularly letter or phonemic fluency (naming as many words starting with a specified letter).

The overall findings regarding within group abilities, indicated that once participants initated HAART, cognitive abilities improved along with their abilities to engage in activities of dailiy living as observed by means of the interview schedule. Theses observed improvements are in keeping with findings from other longitudinal studies using HIV-infected individuals in other parts of the world (Uganda, USA and Australia) ranging from 12 weeks to 18 months (Cohen et al., 2001; Cysique et al., 2009; Lopez et al., 1998; Sacktor, Nakasujja, Skolasky, Robertson, Wong et al., 2006; Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al., 2009).

6.5 Participant Characteristics/Variables that have an effect Cognitive Linguistic Abilities

ANCOVA analysis on the Cognitive Linguistic Quick Test indicated that education significantly effected cognitive-linguistic abilities to perform activities of daily living followed by age and CD4 count. However, the ANCOVA results for the interview schedule showed that age significantly influenced the participants' cognitive-linguistic abilities to perform activities of daily living was age.

The results of the ANCOVA indicated that education and, to a lesser extent, age and CD4 count significantly influenced cognitive-linguistic abilities on the CLQT. These findings were consistent with those reported by Ciccarelli et al. (2011), Singh et al. (2010) and Wong et al. (2007), when they used neuropsychological tests. Ciccarelli et al. (2011) conducted a cross sectional study in Italy that in part investigated the prevalence and treatment correlates of HIV-associated neurocognitive disorders (HAND). They recruited 148 participants, 58% were males, mean age was 46.6 years, mean was

education was 12.5 years, and mean CD4 529. The results of their study indicated that higher education level, CD4 count and age were associated with lower neurocognitive impairments. However, it must be noted that mean education and CD4 counts of participants who initiated HAART in this study were lower than those cited in Ciccarelli et al. Another study with similar results regarding the influence of age and CD4 counts was conducted by Wong et al. (2007). They investigated the frequency of and risk factors for HIV dementia in Uganda by recruiting 78 HIV positive and 100 HIV negative participants in their study. The mean age of the participants was 37, CD4 count was 219, years of education was 8.6 years and there were more females than males. These participant characteristics were very similar to participants recruited for this study. Wong et al. (2007) found that CD4 count and age were significantly correlated with neurocognitive impairments. When Singh et al. (2010) carried out a cross-sectional study in South Africa using 110 HIV positive adults; they found that age and gender correlated with the attention and executive function [Digit Span Backwards, and the Trail Making Tests (Parts A and B)]. The participants in their study were predominantly HIV-infected blacks, predominately female, and with a mean education of 10 years. Their participants' socio-demographics matched the socio-demographics of participants recruited for this study. Below are explanations to suggest why education, CD4 counts and age were significantly associated with cognitive-linguistic abilities in this research.

Education has been closely linked to neurocognitive abilities. It has been shown and substantiated that a person's years of education correlates with cognitive reserve (Groth-Marnat et al., 2000). That is, education results in greater use of brain structures involved in neurocognitive abilities. Education creates experiences that can be drawn upon for novel and previous situations – hence the term cognitive reserve. Therefore it was not surprising that education influenced cognitive-linguistic functioning in this study.

The fact that CD4 counts had some influence on cognitive-linguistic abilities can be explained by in part by the effect of HAART on the viral load. Patients felt better because of the neuroprotective nature of ARVs in suppressing HIV replication and by boosting the number of T-cells, thereby improving the immune function of the body. Kipnis et al. (2008) have hypothesized that the immune system is intimately interwoven with brain function. Hence, immune malfunction may lead to cognitive impairment. According to these authors, the CNS and immune system cannot function optimally without the other; indeed, it is only because of their interactive functioning that the systems can coexist, let alone be of benefit.

Age was also found to have an influence on the cognitive-linguistic abilities of participants in this study. This could have been due to effects of aging on the brain, or others factors such as depression and situational stressors which were not controlled for in this study.

In contrast to the findings of this research Sacktor, Wong, Nakasujja et al. (2005) did not find that education, CD4 counts and age significantly associated with HIV-associated neurocognitive abilities. The difference in findings could be related to the instruments used. Sacktor et al. used the dementia screening scales and not full battery neuropsychological tests to determine the association between variables. Jevtovic et al (2008) also found that age did not significantly correlate with neurocognitive abilities. They examined the incidence of risk factors one of which was age for HIV-associated neurocognitive disorders. They recruited 96 HIV positive patients, 80% were males and 20% were females. Participants were taking HAART and had a mean CD4 count of 141. Their results revealed that having a younger age was not associated with neurocognitive deficits, or older age with dementia. Contrary results regarding the influence of age could have been due to duration of the study, gender differences and the types tests used to assess neurocognitive abilities. Jevtovic et al's

study was cross sectional and there were more males recruited who had a higher education mean than those in this study.

The ANCOVA results of the interview schedule also revealed that age significantly affected or influenced the ability to perform activities of daily living. Studies that used a functional measure such as Sacktor et al (2005) , Sacktor et al (2006), Heaton et al (2010), Ciccarelli et al (2011) did not investigate participant characteristics that may have influenced or had an impact on functional performances. However since age was shown to influence participant cognitive – linguistic abilities to perform activities of daily living in this study; this could have been due to effects of aging on the brain, or others factors such as depression and situational stressors that were not controlled for in this study.

6.6 Reported influence of Cognitive-linguistic Abilities on Activities of Daily Living (ADLs)

The content analysis of the structured interview schedule responses indicated that the cognitive domains of attention, visual spatial and language had some impact on activities of daily living. The results suggested that the longer the participants took ARVs, the less attention and visual problems and language impacted upon ADLs.

The ability to attend to tasks of daily living can be affected by internal and external distracters. Internal distracters are factors that arise from within the individual that affect how an individual attends to ADLs. External distracters would include factors outside of the individual in their environment that would affect how they can attend to a task. For this group of participants internal distracters greatly impacted on their ability to attend to ADLs. The responses indicated that pain was one of the reasons the participants could not effectively engage in everyday activities. These responses concur with

Makoae et al. (2005) and Myezwa et al. (2009), who documented the symptoms experienced by people living with HIV and AIDS in Southern Africa. They reported that their participants complained of joint, abdominal, headache, chest and swallowing pains. Furthermore, since the majority of these patients were either in the third or fourth stage of disease progression before initiation of HAART, it is not surprising that they were experiencing pain (Sarna et al., 1999).

Another internal distractor to attention that was cited by the participants was fatigue. Fatigue is a common symptom in patients with HIV and AIDS; in fact several recent descriptive studies have identified fatigue prevalence rates of 60% (Makoae, 2005; Paddison et al., 2009; Voss, 2005). Fatigue or low energy has been associated with both physical and psychological morbidity (Breibart, McDonald, Rosenfeld, Monkman, & Passik, 1998; Paddison et al., 2009), and poor quality of life (Vosvick et al., 2003). Among HIV-positive patients, disease progression is also related to decreased energy levels (Sarna et al., 1999) that can impose physical limitations on how well activities of daily living are performed (Ferrando et al., 1998).

Still within the domain of attention, the participants felt sad, stressed and angry which is not uncommon for persons with HIV and AIDS to feel (von Gisen, Bäcker, Hefter & Arendt, 2001). The participants in this study felt sad for several reasons. They were sad about their diagnosis and worried about what would happen to their children, and about their finances since most of them were unemployed. According to Brashers, Neidig, Reynolds and Hass (1998), uncertainty is a chronic and pervasive source of psychological distress for persons living with HIV. Depression could also explain why a number of participants at baseline reported that they did not want to socially engage with friends or take part in activities except for religious-related activities. On the other hand, Paul et al. (2005) have suggested that depression is often mistaken for apathy in HIV and AIDS individuals. This is because apathy correlates with direct brain damage especially along the sub-cortical loops whereas

depression does not. Since it has been reported that there is a concentration of the HI virus in the sub-cortical nuclei it is possible for circuitry between the frontal cortex and sub-cortex to be damaged (Berger & Arendt, 2000; Paul et al., 2005). It has already been established that damage to the fronto-striatal circuitry underlies cognitive-linguistic dysfunction observed in persons with HIV and AIDS.

The participants also reported feeling stress and anger. This is not surprising considering that worry and stress tend to go hand in hand. Being worried about children and finances can give rise to undue stress in individuals. Sometimes just knowing that one has a diagnosis of HIV and AIDS is stressful in itself and is further compounded by feelings of anger. The anger was mainly directed at the partners who infected them with HIV.

It was also noted that four months after HAART initiation, pain in the form of headaches, peripheral neuropathy, dizziness and fatigue still persisted despite being reported before HAART initiation. These symptoms are not only HIV-related but could also be related to the effects of HAART such as neurotoxicity (Lewthwaite & Wilkins, 2009; Van Dyk, 2008). The side effects or neurotoxic effects of HAART stopped after four months. The results of this study were similar to those reported by Jelsma et al. (2005), in that HAART was found to greatly improve the physical and mental health of individuals living with HIV and AIDS and the side effects of antiretroviral drugs seemed to have a negligible impact on the well-being of the participants in their study. In fact, after HAART initiation patients reported that they had their lives back and were able to perform activities of daily living that they never thought they could do again (Halikitis, Shrem, Zade & Wilton, 2005).

Participants further reported that they were experiencing dizziness and blackouts. Similarly, Makaoe et al. (2005) also reported that their participants were experiencing these symptoms. This was

probably due to the effects of the HI virus on the CNS. These symptoms disappeared after HAART initiation and were probably due to the positive effects of HAART.

Regarding visual spatial abilities, very few participants indicated that they had visual problems. Some participants reported that they experienced painful eyes and discharge. Other participants reported having eye problems after contracting meningitis and shingles. Makoae et al. (2005) reported that patients in their study complained of blurred vision. Freeman et al. (2008) documented that visual problems experienced by HIV and AIDS patients are not necessarily due to cognitive deficits but are due to retinal dysfunction. This would appear to be the case in this study. No visual problems were reported four and eight months after ARV. This could indicate several possibilities: The participants who indicated that they had visual problems did not return for successive testing, or ARVs were effective in resolving the underlying conditions that had caused the visual problems.

The participants primarily experienced expressive language difficulties in the area of speech. These included vocal quality (hoarse), loudness and rate. These findings are similar to the research of Mathew and Bhat (2008) who found that a few of their participants living with HIV and AIDS presented with difficulties in vocal quality, and loudness. Larsen (1998) also stated that individuals living with HIV and AIDS can present with dysarthria which is a disturbance in speech production caused by damage to the CNS or PNS and which has a resultant negative impact on speech production affecting the speech parameters of respiration, phonation, prosody, resonance and intensity (Duffy, 2005). Loudness problems are usually indicative of respiratory system involvement whereas vocal quality impairments suggest vocal fold involvement (Freed, 2000). These speech problems disappeared after four months of taking HAART. This indicates that whatever was causing the speech problems was due to a compromised immune system. So as the viral load dropped due to the suppressive nature of HAART, the immune system improved as the CD4+ count increased in numbers, thereby warding

off whatever pathogens were causing respiratory and vocal problems. Another explanation could be that the patients who initially reported experiencing speech problems did not return for retesting.

In terms of receptive language, the participants initially reported experiencing hearing difficulties which included not being able to hear, yellowish discharge and ringing in the ears. Hearing loss and yellowish discharge are indicative of two causes - the HI virus itself and opportunistic infections. The HI virus can cause damage to the cochlea, eighth nerve or both, resulting in sensorineural hearing loss, or central auditory disturbance (Kallail, 2008). Opportunistic infections such as otitis media, neurosyphilis, cytpmegalovirus, and crytococcal meningitis can result in some of the following symptoms: tinnitus (ringing in the ear), muffled hearing, and aural fullness (Kallail, 2008; Larsen, 1998). At four and eight months after HAART initiation the participants reported continuing ringing in the ear. This was also reported by Khoza-Shangase (2011) who found that participants living with HIV, three and six months after taking HAART complained of ringing in the ear. This was attributed to the ototoxic effects of HAART, in particular nucleoside reverse transcriptase inhibitors (NRTIs).

Overall the participants' ability to perform activities of daily living appeared to have improved. This was evidenced by a decrease in responses pertaining to cognitive linguistic difficulties that may have affected their ability to conduct activities of daily living. These results were also observed by Sacktor et al. (2006) who conducted a longitudinal study using 23 HIV positive. Part of their study incorporated the use of a functional assessment test- Karnofsky Performance Scale which was used at baseline, three months and six months after HAART use. Improvements were observed at three and six months in the performance functional everyday tasks. Functional abilities improved from being severely impaired to the extent that individuals could not to work to where at the end of six months individuals were able to perform everyday activities of daily living with independence. These results

implied that the effect of time influenced the participants' abilities to perform functional everyday activities. Though the methodology was appropriate in that the participants acted as their own 'controls', functional improvements may have been overestimated in that there was no comparison group to contrast functional improvement.

There is a paucity of research that has investigated how cognitive abilities have impacted upon the ability of HIV-positive individuals to perform activities or participate in their environment within the framework of the ICF. The fact that standardized testing revealed cognitive-linguistic deficits that should have translated to difficulties in performing activities of daily living, but which did not occur, implies fronto-striatal involvement. If the participants had exhibited severe deficits maybe these would have translated to the participants having difficulties conducting activities of daily living (van Gorp, Lamb & Schmitt, 1993). The majority if not all the participants came to the clinic by themselves to get their medical check-ups and refill their HAART prescription using the public transport system. This seems to support the view that activities of daily living are automatic functional activities that are so embedded in long-term memory which does not require new learning and thus individuals do not have to actively process new information in terms of these activities, whereas neuropsychological tests require active participation of higher order thinking skills that rely on working memory and the processing of new information (Koziol & Budding, 2009).

The results of this study revealed that if the researcher had relied solely on the information obtained from the CLQT she would have obtained a detailed description of what was happening with the participants. The researcher would have only collected information pertaining to the biological and not the psychological and sociological aspects of what was happening in their lives. The ICF which was developed from the tenements of the Biopsychosocial model states that it is important to look at all aspects of an individual health condition and not just stop at body structures, function and activities in

the clinical settings. One has to consider participation in terms of activities of daily living and interaction in the participant's environment. Based on the results of the CLQT especially at baseline and four months an assumption could have been made that participants were not effectively performing activities of daily living in their immediate environments. Yet the reports from the interview schedule revealed that they were able to perform activities of daily living even those that involved executive function and memory. Reportedly, participants had developed their own strategies of compensating such as using a phone to remember appointments, or asking family members to assist. Participants reported that internal distracters related to emotions were affecting their ability to effectively attend to activities of daily living. If the researcher had not been guided by the biopsychosocial model of health she would not have obtained a true holistic picture of how HIV-associated neurocognitive deficits present and impact upon an individual living with HIV.

6.7 Demographic Characteristics and Challenges

The clinic where the study was conducted is situated in a government hospital and offers assistance to all individuals from different socio-economic levels. The clinic does not deny anyone access to ARVs based on education or income level. It was believed that the patients at the clinic were a good representative population of urban HIV-infected people. The demographic characteristics of participants in this study were black Africans, mainly female, with a mean age range of mid-thirties to early forties, a mean education of nine years and generally unemployed. The demographics of the participants in this study were comparable to those in a study conducted by Rosen et al. (2008) where HIV-infected individuals were recruited who were accessing care and treatment from public and non-governmental sites. They investigated the characteristics of an HIV-positive urban population in South

Africa and found that more women were diagnosed HIV-positive than men, and the majority of individuals were black aged between the early to mid-thirties, unemployed with some secondary education.

In this study participants had to commit to being tested three times. In order to reduce attrition of participants, testing was done in a time-efficient manner and they were compensated for the transport costs incurred to come back for testing. Due to the high levels of attrition experienced in the study, the number of participants was increased from 80 at the proposal stage to 110. This resulted in the data collection phase lasting 18 months as opposed to 12 months.

There was a high attrition rate of participants from baseline to four months in the experimental group. Ten participants died due to severe illness. Other participants were too ill to travel. A few decided after their first visit that they did not want to be put on a HAART regimen because of the side effects of HAART and they did not feel that they were sick enough to initiate HAART. Some participants also refused to be re-tested either because they had already come to the clinic to refill their prescription and weren't keen to make the journey back to the clinic or they simply refused to be retested. Lastly, the main reasons for participants not returning was due to incorrect contact information. Some had moved to another area and had decided to go to an HIV and AIDS clinic closer to home.

The researcher also found it very difficult to recruit participants for the comparison– HIV-infected but not taking HAART. Attrition was high for this group for the same reasons as those described for the experimental group. Moreover, even though most of the participants had been diagnosed as HIV-positive, they had relatively high CD4 counts that did not meet the inclusion criteria of this research. As a result there were not many patients whom the researchers could recruit. Lastly, the participants' CD4 count made them eligible to initiate ARVs after baseline testing.

In summary, in the context of the high prevalence rates of HIV and AIDS in South Africa it was important to investigate and describe HIV-associated neurocognitive disorders as they appeared in a South African context. Patients were assessed at baseline before HAART initiation and at four and eight months after HAART. Results revealed that the participants did present with deficits in attention, memory, language, executive functions and visual spatial skills at baseline. These deficits, however, improved at each successive testing but did not altogether disappear. Furthermore, even though the participants did exhibit deficits they did self-report that these deficits did not impact greatly on their ability to perform activities of daily living. It was also determined that the variables of education, age and CD4 count influenced their cognitive-linguistic performance on the CLQT**.** Whereas the time of testing and group placement (i.e. HAART use versus non HAART use) were associated with how the cognitive – linguistic abilities impacted upon activities of daily living on the interview schedule.

Chapter 7: Conclusion

7.1 Introduction

In this research a predominantly quantitative approach, i.e. a standardized test – the CLQT, was used together with a structured interview schedule (IS) that was used to compliment the results of the CLQT. The IS was included to obtain a broader and more descriptive understanding of the phenomenon under investigation, namely the effects of HAART on the cognitive-linguistic abilities of adults living with HIV and AIDS. The study was both longitudinal and cross-sectional in nature.

The results of this study draw attention to the fact that South African individuals living with HIV and AIDS present with cognitive-linguistic deficits. It was found in this study that all five of the cognitive-linguistic abilities were affected by the HI virus, the most impaired being the executive function and the least being language at baseline. However, performance in all five cognitive domains improved from baseline to eight months. There was a significant difference in performance between all three groups at different testing times for different cognitive domains. The independent variables of education, age and CD4 count had a significant influence on the cognitive-linguistic abilities for clinical tasks. So too did the variables of time, participant group and age also have a significant influence on the cognitive-linguistic abilities required for activities of daily living. Based on the results of the Cognitive Linguistic Quick Test (CLQT) participants should not have been able to properly perform activities of daily living, but this was not the case. Most of the participants reported that they were able to perform their everyday activities of daily living. When participants were asked to report which cognitive linguistic abilities, if any, influenced their abilities to perform ADLs they cited attention, visual spatial and language, specifically hearing problems. However, their attention and visual difficulties resolved once on HAART but their hearing problems persisted, e.g. ringing in

the ear. Thus, the cognitive-linguistic impairments observed and recorded during testing did not affect how a person conducted their everyday activities.

7.2 Clinical Implications

Results from this study imply that this group of participants presented with cognitive-linguistic deficits that improved with ARV, but did not disappear altogether. These results strongly supported the literature in confirming that the HI virus is able to cross the blood brain barrier and cause irreversible brain and nerve damage (Fernandez, 2005). This information is very important for the clinical management of the patients. Cognitive-linguistic abilities affect adherence to regimen and how information is processed. The fact that the participants presented with mild attention deficits implies that they might experience difficulty attending to complex unfamiliar information, which could lead to information not being processed or comprehended properly. Patients, like the participants in this study, would thus benefit from information being repeated and presented in different ways. If information is repeated and presented visually it would allow the patient enough time for the information to be stored in the working memory so that the executive component - a sub-division of working memory - could manipulate the information so that it could be acted upon. For example, most of the medical and allied health staff are inclined to present all the information verbally and do not utilize strategies that facilitate comprehension. Patients usually complain that they are too scared to ask the nurses or doctors to repeat what they have not understood. So there is a need for verbal messages to be repeated and for the information to be presented visually in pictures or printed in the vernacular. It might be useful for hospitals to employ interpreters because there is an assumption that all Africans in South Africa speak IsiZulu and Sesotho fluently which is not necessarily the case.

According to the results of this study, executive functions do not necessarily affect functional activities of daily living but they have significant bearing on work duties that require some measure of abstraction and executive thinking skills. Nurses and doctors thus need to refer patients for either speech therapy or occupational therapy so that the work environment can be assessed and cognitive therapy can be provided in the context of the work environment.

Participants with HIV exhibited functional language skills in this study. In other words, they were able to express their basic needs and wants. However, the participants presented with language deficits when the context required higher order language skills that were underpinned by cognitive processes such as attention, memory and executive functions. This became apparent when the individuals were presented with complex and unfamiliar information. The individuals may not have readily understood the information presented to them due to minor difficulties in retaining information in their working memory. So it is important that information is verbally repeated and reinforced through other means such as visually printed materials.

The speech problems were not severe as to affect the participants' activities of daily living in terms of influencing interpersonal social interactions; however, their receptive language problems in terms of hearing difficulties were a concern. Therefore, it is important that the patients' hearing be monitored when patients come for their routine check-ups or prescription refills. Patients should be asked if they are experiencing any ear problems that may be affecting their hearing, because of the ototoxic effects of HAART on the structures of the ear. The ability to hear is pivotal to quality of life since it affects how people function socially and at work. Furthermore, HAART has also been reported to cause neurotoxic side effects that can either directly or indirectly, through side effects on other systems, affect the brain (Southern African HIV Clinicians Society, 2008). These neurotoxic side effects can therefore greatly influence an individual's neurocognitive performance. It is thus important

to find cost-effective ways of monitoring the ototoxic and neurotoxic effects of HAART. One such way is through periodically assessing, the cognitive-linguistic abilities of HIV-infected individuals on HAART by using the Cognitive Linguistic Quick Test.

7.3 Research Implications

It is important that allied health professionals especially speech language pathologists and neuropsychologists do not to only rely on standardized tests to diagnose the cognitive abilities of individuals living with HIV and AIDS. This is because standardized tests do not necessarily provide a holistic picture of the clients' abilities. The client's impairment should be viewed through the framework of the ICF's definition of disability since it has already been established that HIV and AIDS can be termed a disability. Furthermore, a diagnosis of cognitive-linguistic deficits needs to be viewed in the light of how it impacts upon the individual's functioning in the context of their activities and participation in their immediate environment.

Moreover, both the Cognitive Linguistic Quick Test (CLQT) and the structured interview schedule (IS) highlighted the fact that the participants did not exhibit dementia, based on the mean raw scores of the CLQT and the IS. The scores indicated that the participants exhibited asymptomatic neurocognitive impairments (ANI) or minor cognitive motor disorders (MCMD). In fact, the participants exhibited deficits in two or more cognitive domains, but the deficits were not severe enough to prevent the participants from performing their everyday tasks.

Based on functional MRI observations (Melrose et al., 2008) and the findings of this research and others (Woods et al., 2004), fronto–striatal functioning was deemed to be compromised in patients with HIV. This was confirmed by the participants' difficulties in phonemic cueing and

performing tasks that relied heavily on working memory, executive function and visual spatial skills. The latter are tasks that are dependent on intact cortical-subcortical circuits. Therefore it is it important that the cognitive-linguistic assessment of individuals with HIV and AIDS not only include simple cortical abilities but also tap into higher order thinking skills. If this is not done many individuals with HAND may go undiagnosed because the tests used for assessment were not sensitive enough to detect the subtle and minor cognitive-linguistic deficits.

HIV-associated neurocognitive disorders (HAND) are often overlooked by busy healthcare providers. So a validated instrument such as the Cognitive Linguistic Quick Test should be included in the regular clinical assessment of people with HIV and AIDS, particularly in the case of the most vulnerable patients such as those with low CD4 cell counts. It is thus important that they are diagnosed and monitored for several reasons: (i) they are associated with an increased risk of mortality (Grant et al., 2005); (ii) the presence of HAND can affect antiretroviral therapy adherence which is essential for the suppression of virological replication (Solomon & Halikitis, 2008; Ettenhoffer et al., 2010); (iii) HAND and HAD have been shown to be treatable, i.e. improve with HAART as demonstrated in this study and others (Cohen et al. 2001; Sacktor, Nakasujja, Skolasky, Robertson, Musisi et al., 2009); (iv) The diagnosis of HIV-associated neurocognitive disorders can be an indication for the initiation of antiretroviral therapy which could have enormous benefits for the individuals themselves, their families and their communities. Moreover, it has been suggested that memory impairments can also alert clinicians to the possibility of brain disease (Panegyres, 2004).

The results of this research suggested the presence of on-going brain atrophy in HIV-positive patients taking HAART evidenced by the continued presence of neurocognitive impairments. This raises the possibility that these patients may be at a greater risk for future cognitive impairments and

dementia (Cardenas et al., 2009). These findings further lend support for on-going assessment and monitoring of HAND.

In terms of improving the quality of life of individuals living with HIV and AIDS in South Africa, there needs to be a more integrated approach to the treatment of HIV and AIDS. Management of these patients needs to encompass a more holistic approach that includes more allied health professionals besides nurses, doctors and social workers, but also speech therapists, occupational therapists, even traditional health practitioners, as well as the patients themselves. In this way patients can be treated more effectively in line with the tenets of the ICF. This framework of treating individuals with HIV and AIDS would most probably greatly assist in curbing severe forms of HAND and other HIV conditions.

7.4 Limitations and Future Research

This study had a number of limitations that may have impacted on the results obtained in this research. Following will be a discussion of these:

7.4.1 Assessment

Most neuropsychological tests appear to be sensitive to cortical damage, but the Cognitive Linguistic Quick Test has proven to be sensitive to both cortical and fronto-striatal damage in this study in that it was able to detect both executive functions and language abilities that were heavily reliant on cognitive abilities such as working memory and long-term memory. Therefore, a more comprehensive, in-depth battery of tests was not deemed necessary. Other reasons for not using a

battery of tests were that they were too expensive and time-consuming to conduct on a large number of participants. Since initial testing occurred in the latter stages of the progression of HIV and AIDS the researcher needed to perform a test that would take into consideration the stamina and alertness levels of the participants. Ultimately a balance was struck between using a test such as the CLQT that was sensitive enough to detect asymptomatic neurocognitive impairments and which was not too time-consuming to conduct.

The same instruments, that the Cognitive Linguistic Quick Test and the interview schedule, were used on the same groups of participants at all three testing periods; to ensure that that responses or outcomes of testing could be attributed in the most part to HAART intervention and not to the use of other tests. In an effort to rule out practice effects the results of the longitudinal group were compared to those of the cross-sectional group. The cross-sectional group included different individuals at baseline, four and eight months that had not been exposed to the CLQT or structured interview schedule. The results for both the longitudinal and cross-sectional groups yielded similar results. It was therefore cautiously assumed that any improvements observed in cognitive-linguistic abilities were due to the effects of HAART and not to practice effects.

Though the structured interview served to provide more information about the participants' activities of daily living it only dealt with an aspect of quality of life. A detailed quality of life assessment that covered more factors of the ICF in relation to cognitive - linguistic abilities could be useful in under resourced areas; especially in regards to management of individuals living with HIV and AIDs. Lastly in regards to assessment, the participants' exposure or experience to neurocognitive testing may have influenced their test scores. Even though a pilot study was conducted the participants' familiarity and novelty of CLQT could still have been confounding variable(s).

7.4.2 Confounding variables

Despite the corrective measures put in place to control for threats to reliability, certain confounding variables could not be controlled, for instance compliance with or adherence to HAART. It was assumed that the participants were adhering to HAART even though questions were not asked regarding adherence. The observed improvement in the participants' cognitive-linguistic abilities after initiation of HAART suggested adherence to medication. According to Ettenhofer et al. (2010), medication adherence significantly predicts neurocognitive performance.

Consultation with other forms of healers and the use of "mbejane" (traditional herbal medicine) before and after treatment could also not be controlled for. It is likely that some participants had used "mbejane" before consulting western medical practitioners. According to Gilks (2001), it is not uncommon for individuals living with HIV to use home remedies and traditional healers to treat their symptoms. The ARVs prescribed in the triple cocktail or HAART for the participant, or the type of diet(s) participants were eating in terms of maintaining optimal health, were also difficult to control for. Lastly the researcher could not regulate the drugs prescribed in conjunction with antiretrovirals (ARVs) to treat concurrent opportunistic infections and diseases or conditions caused by the side effects of HAART.

In another attempt to control for confounding variables a matched comparison group was recruited as opposed to a 'true' matched control group. Initially the researcher attempted to recruit a matched control group but due to variables beyond the researchers the control group developing into a comparison. Even the recruitment of the comparison group was very difficult to do due to the issues discussed earlier of individuals electing to start HAART, or them not meeting the CD4 count

requirement. So due to the comparison group sample size being so small, CD4 count differences and their clinical presentation of the disease (asymptomatic versus asymptomatic), comparison between the two groups of participants' (i.e. experimental and comparison) could not have been conclusive. Hence the recruitment of a cross sectional group which served as a reference comparison group. This allowed a comparison between groups to be done and weakened the argument for practice effect.

Depression, apathy, fatigue were not assessed or controlled for due to time and financial constraints. For example depression can cause pseudo cognitive deficits. The use of imaging technique(s) along with the depression measures could have been done bolstered the results; since at baseline the participants reported feeling sad. However, these responses decreased upon successive testing. This is an important area to investigate for future studies looking at neurocognitive deficits in a South African population.

This was an exploratory study and more studies are needed to further substantiate what independent variables (gender, race, employment, economic status and education) influence cognitive – linguistic abilities before we can generalize across cultures, gender and other independent variables. Lastly, since neurocognitive impairments were observed over time, this suggests that sustained HAART treatment may be necessary to produce optimal neurocognitive benefit. Prospective studies controlling for HIV duration, HAART treatment regimen, adherence and duration of HAART use are needed to examine what their independent contributions are to the observed effects.

7.4.3 Sample size

In relation to sample size the sample sizes for three groups were deemed small but sufficient for the context. Ideally a larger group, using more government clinics in the region would be

recommended. This study was both exploratory and descriptive in nature and therefore was focused on one clinic using convenient sampling procedures. The latter could have influenced the generalizability of results and statistical significance of results. To increase sample size, future research may need to include several sites for comparison of cognitive-linguistic abilities across different South African cohort populations.

For example, this research used a cohort from a government urban hospital. The question is thus - would the results have been similar if the cohorts had been from rural district hospitals, private clinics or even other government urban clinics? Presumably private clinics would yield a different set of demographics as compared to public clinics, e.g. a more educated cohort of participants. Since participants yielded mild to severe deficits across all five cognitive domains at baseline that improved after HAART use, further research is warranted to explore how and to what extent individuals compensate for early cognitive-linguistic impairment and gradual decline. This research also relied on standardized testing and an interview schedule to determine the extent of cognitive-linguistic impairments. However, the use of quantitative magnetic resonance imaging procedures for determining the effects of HAART on HIV-associated neurocognitive disorders might lead to interesting discoveries that could aid treatment.

7.4.4 Strengths

Limitations notwithstanding, the greatest strength of this study was the fact that it was both longitudinal and cross-sectional in design. The use of both designs allowed for some comparisons to be made regarding the effects of HAART and reduced the possible effects of some of the confounding variables such as age, gender, education, and practice effect.

Another strength of this study was the use of two different but complimentary methods that highlighted the same phenomena of investigating cognitive-linguistic abilities of individuals living with HIV and AIDS. The Cognitive Linguistic Quick Test (CLQT) was able to provide information regarding clinical cognitive-linguistic performance and confirm the hypotheses. It was deemed an efficient and reliable test for monitoring the effects of HAART on cognitive-linguistic abilities of individuals living with HIV and AIDS. Since the HIV positive sample in this study was recruited from a voluntary counselling and testing clinic, and an ARV outpatient clinic, assessment needed to be time efficient and inexpensive - which it was. Participants could complete the test relatively quickly so that they were able to re-join the queue without losing their place for either counselling, treatment and/or prescription pick-up. The test was considered to be reliable, thorough and sensitive enough to detect a range of cognitive-linguistic deficits ranging from mild to severe. Furthermore, the CQLT was found to represent a good balance between longer, but less practical batteries and shorter but less sensitive screening tests. Moreover, the test could be used by other trained allied health professionals besides speech pathologists and psychologists. Due to the cognitive – linguistic results obtained from the CLQT, it was found suitable for use in monitoring the neurocognitive abilities of individuals living in under resourced settings in South Africa.

It was within the framework of the ICF that the researcher found it important to not only assess and document the severity of HIV-associated neurocognitive disorders/cognitive-linguistic impairment exhibited by the patients before and after HAART use, but also to investigate whether these neurocognitive impairments influenced a person's activity and participation in activities of daily living (ADLs). This could only be achieved by conducting an interview schedule that allowed the individuals to self-report on how cognitive impairments were affecting their everyday activities. Though neuropsychological tests can provide information about the severity of an individual's

neurocognitive deficits, they cannot conclusively describe how these deficits influence a person's quality of life in terms of their activities and participation in their environment. The -structured interview schedule provided more in-depth information than the CLQT on how the cognitive-linguistic deficits influence activities of daily living.

The interview schedule was able to provide information on how cognitive-linguistic impairments were impacting upon activities of daily living. The participants' performance on the CLQT did not necessarily reflect how participants were able to perform their activities of daily living. The results from the interview schedule showed that while activities of daily living improved after HAART initiation, most of the participants were still able to carry out their functional activities prior to HAART initiation. Therefore even though the CLQT indicated cognitive – linguistic deficits, they did not tell the whole. The participants were still able to carry out their activities of daily living despite having impairments. Despite the limitations of this study, the results of the study were able to reveal that cognitive-linguistic deficits do improve but do not completely disappear when an individual is taking HAART.

7.5 Concluding comments

The Biopsychosocial model of disease states that as health professionals we need to look at a health condition in terms of how it interacts with the biological, psychological and sociological factors (Engel, 1980. This study in some measures was able to embrace that by not only investigating the biological aspects but also the psychological and to a minimal extent the sociological. This study followed the ICF framework which is undergirded by the biopsychosocial model (BM) (WHO, 2010).

The biological factor of the biopsychosocial model encompasses the body structures and parts of body functions of the ICF. The literature review showed that for an individual living with HIV to present with HIV-associated neurocognitive disorders the HI virus will have entered the CNS and caused damage to the brain cells (Eugenin et al., 2006). Imaging studies and the theory of cortical-subcortical circuitry were presented to substantiate the latter premise (Ernst, 2003; Murdoch & Whelan, 2009; Thompson et al., 2006). When structures of the CNS in particular the brain are affected certain body functions are impaired. In the case of this study those were the cognitive – linguistic abilities under investigation - attention, language, visual spatial skills, memory and executive functions. The body functions were assessed using the Cognitive Linguistic Quick Test. The body's diseased structures were treated using HAART.

Psychological factor that included aspects of body function, activities and participation features of the ICF were also affected by HAND in terms of the participants' abilities to perform activities of daily. The psychological factor was assessed using the structured interview schedule. The assessment revealed from the responses obtained that participants deal with personal and physical issues before and sometimes after treatment. Treatment for this was HAART. The sociological factor that included aspects of the ICF (environmental and personal contexts) were also impacted by HAND. Some of the questions from the structured interview schedule obtained information regarding how activities of daily living impacted upon the participants' immediate environment and personal relationships. The overall results obtained from the interaction of the three factors of the BM appeared to show that HAART improves the cognitive-linguistic abilities of adults with HIV and AIDS and their ability to perform activities of daily living.

This topic is and will continue to be of substantial relevance to the further understanding and treatment of HIV. The results of this study will add to the current body of knowledge on

neurocognitive deficits in HIV patients living in South Africa and can be used to enhance current intervention strategies as well as inform the development of new programmes in the management of individuals with HIV and AIDS. If health care providers were made aware of neurocognitive deficits in their patients, they could start incorporating adherence techniques and memory strategies that patients could use at home and at work to improve their lives. Neurocognitive tests along with a functional measure are useful tools that should be incorporated into routine check-ups and that can be carried out by primary healthcare providers fairly easily with little cost attached, but with potentially important benefits for the patient.

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APPENDICES

Appendix I - Ethical Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mupawose

CLEARANCE CERTIFICATE	PROTOCOL NUMBER M070201
PROJECT	The Effects of Antiretroviral Therapy on the Language and Communication of Comptence of Adults Living with HIV/AIDS Attending ar
INVESTIGATORS	Mrs A Mupawose
DEPARTMENT	SHCD/Speech Pathology
DATE CONSIDERED	07.03.02
DECISION OF THE COMMITTEE*	APPROVED UNCONDITIONALLY

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

UNIVERSITY OF THE WITWATERS PROF AJ WOODIWISS Co-Chair 2007 -10- 15 HREC (Medical) JOHANNESBURG

DATE 07.09.14 CHAIRPERSON .....
(Professors PE Cleaton-Jones, A Dhai, M V
C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof E Ross

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floo Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovemer research and I/we guarantee to ensure compliance with these conditions. Should any departure to b contemplated from the research procedure as approved I/we undertake to resubmit the protocol to t Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mupawose

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M070201**
PROJECT	To Investigate the Cognitive and Linguistic Abilities of Adults Living with HIV/AIDS before and After Antiretroviral Therapy (new title)
INVESTIGATOR	Mrs A Mupawose
DEPARTMENT	SHCD/Speech Pathology
DATE CONSIDERED	07.03.02
DECISION OF THE COMMITTEE*	APPROVED UNCONDITIONALLY

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

DATE 09.02.18 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof E Ross

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 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.**

Appendix II - Permission to conduct research

University
of the Witwatersrand,
Johannesburg

Clinical HIV Research Unit, Department of Internal Medicine

SECRETERIAT: Suite 176, Private Bag x2600, Houghton 2041, South Africa • Tel: +27-11-276-8800 • Fax: +27-11-482-2130

Anniah Mupawose
Department of Speech Pathology and Audiology
University of the Witwatersrand

18 January 2007

Dear Anniah,

THE EFFECTS OF ANTIRETROVIRAL THERAPY ON THE LANGUAGE AND COMMUNICATION COMPETENCE OF ADULTS LIVING WITH HIV/AIDS ATTENDING AN OUT-PATIENT CLINIC IN GAUTENG, SOUTH AFRICA

Thank you for sharing your research proposal with us and for selecting the Themba Lethu Clinic at Helen Joseph Hospital as the site for your research. Your proposal has been reviewed by Dr Denis Rubel, Head of the Themba Lethu Clinic, and me and we hereby give permission for you to conduct this research in the Clinic and in the Clinical HIV Research Unit.

This permission is subject to the following conditions:

1. Your protocol and the necessary consent forms must be approved by the Human Research Ethics Committee: (Medical) of the University of the Witwatersrand before you start recruiting participants at the clinic.
2. Copies of the document giving approval from the Human Research Ethics Committee: (Medical), consent forms and your final research proposal must be sent to Marlene Naidoo at the Clinical HIV Research Unit. (manaidoo@witshealth.co.za)
3. You will be required to make a presentation at a meeting of the Clinical HIV Research Unit on the background and the objectives of the research within three months of commencing recruitment and again on the results once the research has been completed. These meetings will be part of the regular academic programme of the Clinical HIV Research Unit and usually last about an hour.

4. Acknowledgement of Right to Care, Themba Lethu Clinic and the Clinical HIV Research Unit must be made on all published materials and copies of these must be sent to the Clinical HIV Research Unit (Marlene Naidoo, manaidoo@witshealth.co.za).
5. While the staff of the Themba Lethu Clinic and the Clinical HIV Research Unit will do all they can to assist you in conducting your research, they cannot be expected to neglect their duties at the clinic in favour of your research. For this reason you are advised that regular assistance, such as language interpretation, must be provided by you.
6. It is expected that all information relating to patients in the Clinic will remain confidential and that the identity of patients will not be revealed to any third parties or in any publication. A statement to this effect must appear in all consent forms.

We look forward to working with you and please do not hesitate to discuss any aspect of your research in the Clinic with us.

Yours sincerely,

Prof A P MacPhail MBBCh PhD FCP FRCP
Professor Emeritus
Professorial Research Fellow
Clinical HIV Research Unit
Department of Medicine

Dr Dennis Rubel MBBCh DTM&H
Head, Themba Lethu Clinic
Helen Joseph Hospital

Appendix III - Information and consent sheets

INFORMATION SHEET

Hello, my name is Anniah Mupawose and I am a university lecturer. I am currently studying for my postgraduate degree at the University of the Witwatersrand. As part of my research work, I am investigating the language functions of adults living with HIV/Aids before and after receiving antiretroviral therapy.

I would like to invite you to participate in my study, by answering questions concerning your language and communication abilities and how they may have affected your quality of life. This will take approximately30 minutes. If you agree, your responses will be videotaped to allow for observing your communication behaviours. However the video tapes will be destroyed after completion of the study.

Participation in the study is entirely voluntary. There will be no negative consequences if you do not wish to participate and your treatment at the hospital will not be affected in any way. If you choose to participate, you may withdraw from the study at any time.

If you choose to take part you will be assisting me to gain insight and knowledge about the thinking and communication skills of people living with HIV/Aids before and after receiving antiretroviral therapy.

If you agree to take part in the study, I will also require permission to refer to your medical files for your medical history, and CD4 count. All information will be kept confidential and will be reported on anonymously in my research report. Your name will not be used in the study; instead a number will be used. This is to ensure that nobody will know you were a part of this study.

If you wish to be informed of the results in this study, please feel free to request the results and these will be provided to you.

If you are concerned about anything in the questionnaire, or wish to discuss anything with me, please feel free to do so. If you have any further queries, please do not hesitate to contact me on 082 351 9410

Thank you for taking the time to consider participating in my study.

Anniah Mupawose

CONSENT FORM

I, _____ am willing to participate in this study. The study procedures and my rights as a research participant have been explained to me in full, and understand her explanation. The questions I have asked were answered to my satisfaction. I understand that my participation is entirely voluntary and that I can stop participating in the study at any time should I wish to do so.

_____ _____

Participant's Signature **Date**

Consent Form to Review Medical Records

I hereby confirm that I give consent for the researcher to review my medical records as part of the data collection for her PhD research. It has been explained to me that the information collected by the researcher Anniah Mupawose will serve to add information to her research on the language functions of adults living with HIV/Aids before and after antiretrovirals. I understand that efforts will be made to conceal my identity, and that full anonymity will be guaranteed

I understand that I may view the material obtained by arrangement with Anniah Mupawose. However, once the material is made available for research, I realize that recovery of the material may not be possible.

I confirm that the purpose for which the material may be used has been explained to me in terms which I have understood. It has been made clear to me that refusal to consent will in no way affect my medical care. I confirm that I am over 16 years old, of sound mind and that I am not signing under any form of duress.

In the space at the bottom of this letter please indicate whether you want or do not want your medical records to be reviewed

_____

I do/do not give permission for them to be reviewed

_____ Date

_____ Signature

Appendix IV - Interpreter's confidentiality form

INTERPRETER'S CONFIDENTIALITY FORM:

I, _____ understand the purposes and procedures of the study and I promise that I shall not divulge any information that I may learn in my capacity as an interpreter for this project.

_____ _____

Signature **Date**

COGNITIVE LINGUISTIC QUICK TEST

CLQT

Cognitive Linguistic Quick Test

Record Form

Name: _____ ID Number: _____

Address: _____

Phone Number: _____ Years of Education: ____

Present/Former Occupation: _____ Marital Status: _____

Gender: Male ○ Female ○ Handedness: Left ○ Right ○

Native Language: _____

Languages Spoken: _____

Primary Diagnosis: _____

Date of Onset: _____

Hemiparesis: Yes ○ No ○ Side of Hemiparesis: Left ○ Right ○

Severity of Hemiparesis: Mild ○ Moderate ○ Severe ○

Site of Brain Lesion(s): _____

Other Medical Problems: _____

Current Medication(s): _____

Examiner's Name: _____

Referral Source: _____

Contact Person: _____

Phone Number: _____

Relationship to Examinee: _____

Dates	Year	Month	Day
Date Tested			
Date of Birth			
Age			

Severity Ratings Summary

Cognitive Domain	Severity Rating
Attention	WNL* Mild Moderate Severe
Memory	WNL Mild Moderate Severe
Executive Functions	WNL Mild Moderate Severe
Language	WNL Mild Moderate Severe
Visuospatial Skills	WNL Mild Moderate Severe
Composite Severity Rating	WNL Mild Moderate Severe
Clock Drawing Severity Rating	WNL Mild Moderate Severe

*Within normal limits

Qualitative Observations

Describe the presence of perseveration, response delay, self-correction, "set" problems, cooperation, need for prompts, no response, unintelligibility, or other observations. See Chapters 3 and 4 for more information.

THE PSYCHOLOGICAL CORPORATION®

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To reorder CLQT Record Forms, ☎: 1-800-872-1726

ISBN 015-4328-04-9

9 780154 328045

General Administration Directions

1. Administer the tasks in the order in which they appear on the *Record Form*.
2. Refer to the *Examiner's Manual* for detailed administration and scoring directions and examples.
3. Say directions printed in **dark blue** to the examinee. Use a normal conversational rate and stress pattern.

Personal Facts

Stimulus Manual	Response Booklet	Additional Materials	Probes	Repetitions	Time Limit
N/A	N/A	None	Provided for individual items	You may repeat each item 1 time.	N/A

Directions: Administer each item in the order listed. Do not allow the examinee to use reminders (e.g., calendar, address book). Repeat the item if requested or if there is no response after 10 seconds.

Say, **"I want to check some facts."**

Probes: Probes are listed after items 1, 2, and 4. Administer once if the examinee gives an incomplete response or does not understand the item.

Recording and Scoring: Write the examinee's response to each item and circle the score. Circle one or more of the descriptions if applicable.

Item	Response	Score: Correct	Score: Incorrect	Description: 5-Second Delay	Description: Self-Corrected	Description: Probe Needed	Description: Perseveration	Description: Unintelligible	Description: No Response
1. "When were you born?" (For incomplete responses, probe for month, day, or year.)	Month	1	0	5D	SC	PR	P	UN	NR
	Day	1	0	5D	SC	PR	P	UN	NR
	Year	1	0	5D	SC	PR	P	UN	NR
2. "Where were you born?"* (For incomplete responses, probe for the city or state [country].)	City	1	0	5D	SC	PR	P	UN	NR
	State (Country)								
3. "What is your age now?"	Age	1	0	5D	SC	PR	P	UN	NR
4. "What is your complete current address?" (For incomplete responses, probe for the street, city, or state. No ZIP code is needed.)	Number & Street	1	0	5D	SC	PR	P	UN	NR
	City	1	0	5D	SC	PR	P	UN	NR
	State	1	0	5D	SC	PR	P	UN	NR

* The examinee must state both the city and state (country) to receive 1 point. If you don't know the examinee's city and state (country) of birth, score 1 point for a plausible response.

Personal Facts Item 4

Clinician's Note

This task helps to assess memory and language abilities. Examinees with aphasia may respond poorly to the items due to language problems. In such cases, the memory severity rating may not accurately reflect memory skills. Note whether examinees demonstrate better recall of lifelong facts (date and place of birth) vs. newer facts (current age and address), a pattern seen especially in individuals with dementia and closed head injury. Delayed and/or self-corrected responses may indicate milder memory problems.

Symbol Cancellation

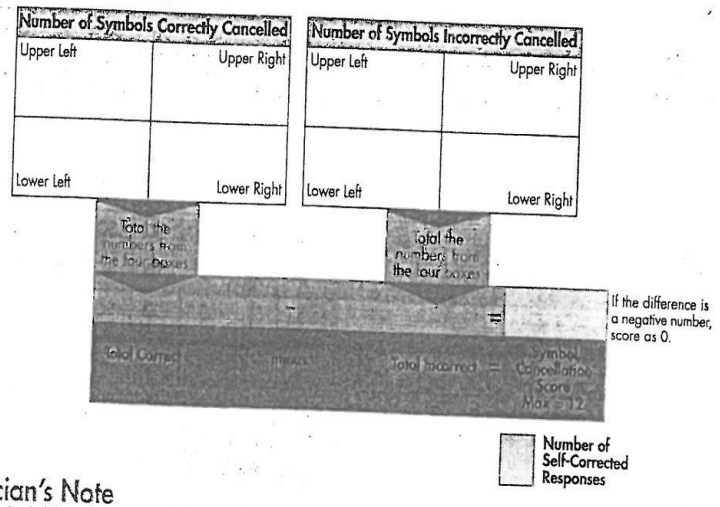
Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Pages 1–2	Pen for examinee, Symbol Cancellation Scoring Transparency	Prompt to encourage task completion.	You may repeat the directions 1 time.	2 minutes

Directions: Open the *Response Booklet* so that pages 1 and 2 are facing the examinee. Present the demonstration item on page 1. Say, **"Look at this symbol.** (Point to the target symbol on page 1.) **This symbol appears several times on this page.** (Point to page 2 of the *Response Booklet*.) **Point to one.** (Wait for the examinee's response. Correct an incorrect response by pointing to a symbol near the center of the page.) **I'm going to cross out the symbol."** Go back to page 1 and place an X on the symbol on the Demonstration Item that matches the target symbol.

Say, **"Now, I want you to cross out every example of this symbol** (point to the target symbol on page 1) **on this page** (point to page 2). **Do you have any questions?** (Repeat the instructions if necessary.) **You have 2 minutes.** (Give the examinee a pen.) **Start now."** Leave page 1 in view and begin timing.

Prompts: If the examinee abandons the task before completion, encourage him or her to continue (until the 2-minute deadline) by saying something like, **"Keep going; you have time left,"** or **"Are you finished? Go back and check your work."** Do not provide any information regarding the accuracy of the responses and do not prompt for missed targets.

Recording and Scoring: Use the Symbol Cancellation Scoring Transparency to determine correctly and incorrectly cancelled symbols by quadrant. Record the numbers in the appropriate boxes below.



Clinician's Note

Symbol Cancellation is a nonlinguistic task of visual attention and perception. It also offers information regarding the integrity of the upper and lower quadrants of left and right visual fields. Observe examinees' scanning strategies. Are they searching laterally from left to right, down and up, or scanning unsystematically? Notice if examinees failed to cancel symbols in one or more of the four quadrants. Errors of omission (correct symbols not cancelled) and commission (incorrect symbols cancelled) may be secondary to: 1. generalized inattention, 2. visual discrimination problems, 3. partial or full hemianopsia, 4. visual neglect, or 5. inattention to one side or quadrant of space. Observe whether there are similar visual field deficits on Clock Drawing, Symbol Trails, and Mazes tasks. See Chapter 3 in the *Examiner's Manual* for more information.

Confrontation Naming

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
Pages 1–10	N/A	None	Prompt for a "common name" or a single-word response.	You may repeat the directions 1 time for each item.	30 seconds per item

Directions: Say, **"Now, I want you to name some pictures."** Turn to page 1 of the *Stimulus Manual* and prese the first picture and say, **"What is this?"** Then present the remaining pictures (pages 2–10). You may say, **"Wh is this?"** or **"...and this one?"** as you present each picture.

Prompts: If the examinee gives a seldom-used word (e.g., "four-in-hand"/tie), ask for the common name. If the examinee gives an elaborated response (e.g., banana with peeling), ask for a single word. Do not provide additional prompts or probes.

Recording and Scoring: Record incorrect responses verbatim. Circle 1 point for a correct response, an acceptab variation of a correct response, a dialectal variation, or a commonly accepted synonym for the stimulus. Circl ½ point if the examinee produces at least half of the phonemes or syllables correctly. Give no credit for respon that have less than half of the phonemes or syllables correct. Circle one or more of the descriptions if applicab

Item	Response	Score			Description				
		Correct	Half Correct	Incorrect	5-Second Delay	Self-Corrected	Perseveration	Unintelligible	No Respo
1. cow		1	½	0	5D	SC	P	UN	NR
2. chair		1	½	0	5D	SC	P	UN	NR
3. (eye)glasses		1	½	0	5D	SC	P	UN	NR
4. hammer		1	½	0	5D	SC	P	UN	NR
5. (neck)tie		1	½	0	5D	SC	P	UN	NR
6. train		1	½	0	5D	SC	P	UN	NR
7. chicken/hen/rooster		1	½	0	5D	SC	P	UN	NR
8. banana		1	½	0	5D	SC	P	UN	NR
9. shirt		1	½	0	5D	SC	P	UN	NR
10. zipper		1	½	0	5D	SC	P	UN	NR

Clinician's Note

Deficits in confrontation naming are a key symptom of aphasia that can result from various forms of brain damage (e.g., stroke, head inju dementia, tumors, infections). Delayed responses suggest mild-word-retrieval problems. Note immediate or delayed perseverations (repeat responses) of all or part of a previous word. Although no points are deducted, an elaborated response may be symptomatic of verbosity c inability to limit information. Ask the examinee to give a single word response. Use of seldom-used words may be a symptom of word-find problems. Request a "common name." The types of errors examinees make can guide treatment of word-retrieval problems. See Chapter 3 the *Examiner's Manual* for various types of naming errors that may provide differential diagnostic information.

bol Cancellation

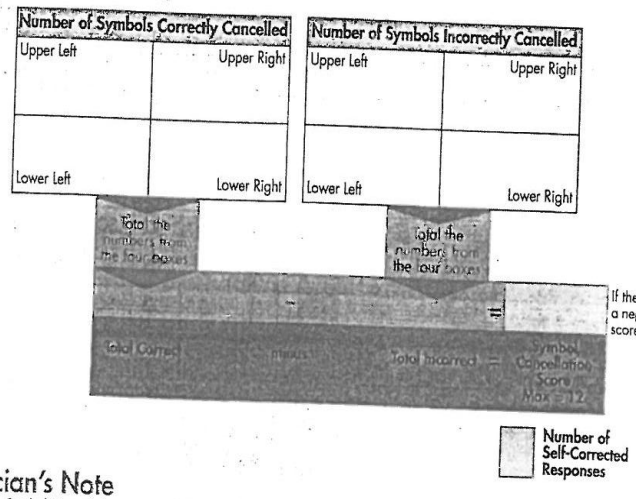
Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Pages 1–2	Pen for examinee, Symbol Cancellation ScoringTransparency	Prompt to encourage task completion.	You may repeat the directions 1 time.	2 minutes

Directions: Open the *Response Booklet* so that pages 1 and 2 are facing the examinee. Present the demonstration item on page 1. Say, **"Look at this symbol.** (Point to the target symbol on page 1.) **This symbol appears several times on this page.** (Point to page 2 of the *Response Booklet*.) **Point to one.** (Wait for the examinee's response. Correct an incorrect response by pointing to a symbol near the center of the page.) **I'm going to cross out the symbol."** Go back to page 1 and place an X on the symbol on the Demonstration Item that matches the target symbol.

Say, **"Now, I want you to cross out every example of this symbol** (point to the target symbol on page 1) **on this page** (point to page 2). **Do you have any questions?** (Repeat the instructions if necessary.) **You have 2 minutes.** (Give the examinee a pen.) **Start now."** Leave page 1 in view and begin timing.

Prompts: If the examinee abandons the task before completion, encourage him or her to continue (until the 2-minute deadline) by saying something like, **"Keep going; you have time left,"** or **"Are you finished? Go back and check your work."** Do not provide any information regarding the accuracy of the responses and do not prompt for missed targets.

Recording and Scoring: Use the Symbol Cancellation Scoring Transparency to determine correctly and incorrectly cancelled symbols by quadrant. Record the numbers in the appropriate boxes below.



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Pages 1–10	N/A	None	Prompt for a "common name" or a single-word response.	You may repeat the directions 1 time for each item.	30 seconds per item

Directions: Say, **"Now, I want you to name some pictures."** Turn to page 1 of the *Stimulus Manual* and prese the first picture and say, **"What is this?"** Then present the remaining pictures (pages 2–10). You may say, **"Wh is this?"** or **"...and this one?"** as you present each picture.

Prompts: If the examinee gives a seldom-used word (e.g., "four-in-hand"/tie), ask for the common name. If the examinee gives an elaborated response (e.g., banana with peeling), ask for a single word. Do not provide additional prompts or probes.

Recording and Scoring: Record incorrect responses verbatim. Circle 1 point for a correct response, an acceptab variation of a correct response, a dialectal variation, or a commonly accepted synonym for the stimulus. Circl ½ point if the examinee produces at least half of the phonemes or syllables correctly. Give no credit for respo that have less than half of the phonemes or syllables correct. Circle one or more of the descriptions if applicab

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4. hammer		1	½	0	5D	SC	P	UN	NR
5. (neck)tie		1	½	0	5D	SC	P	UN	NR
6. train		1	½	0	5D	SC	P	UN	NR
7. chicken/hen/rooster		1	½	0	5D	SC	P	UN	NR
8. banana		1	½	0	5D	SC	P	UN	NR
9. shirt		1	½	0	5D	SC	P	UN	NR
10. zipper		1	½	0	5D	SC	P	UN	NR

Clinician's Note

Deficits in confrontation naming are a key symptom of aphasia that can result from various forms of brain damage (e.g., stroke, head inju dementia, tumors, infections). Delayed responses suggest mild-word-retrieval problems. Note immediate or delayed perseverations (repea responses) of all or part of a previous word. Although no points are deducted, an elaborated response may be symptomatic of verbosity c inability to limit information. Ask the examinee to give a single word response. Use of seldom-used words may be a symptom of word-find problems. Request a "common name." The types of errors examinees make can guide treatment of word-retrieval problems. See Chapter 3 the *Examiner's Manual* for various types of naming errors that may provide differential diagnostic information.

Clock Drawing

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Page 3	Pen for examinee	Prompt to encourage task completion.	You may repeat directions 1 time.	3 minutes

Directions: Place page 3 of the *Response Booklet* and a pen in front of the examinee. Say, **"I want you to draw a clock on this page.** (Point to the directions at the top of page 3.) **First, put all the numbers inside the circle. Then, set the hands to '10 minutes after 11.' Be careful. Be neat. Start now."** Begin timing. Do not allow the examinee to look at a clock or watch.

Prompts: If the examinee stops working before the task is completed and time remains, say, **"Is that all?"** or **"Are you finished?"** If all numbers are omitted, remind the examinee to include numbers. If necessary, prompt the examinee to write Arabic numerals (no Roman numerals). If the examinee draws a third hand, point to the third hand (after completion of the clock) and ask, **"What is this?"** to determine if it is a hand indicating seconds, a self-corrected hand, or an extra hand.

Recording and Scoring: Score each element of the clock separately. Circle the score for each element and place a check in a box if appropriate. Make allowances for use of a non-dominant hand.

Score

1. How many numbers are present? Are they legible in context? 3 2 1 0
   - 3 = Numbers 1–12 are present with no perseverated or extra numbers.
     - ☐ Check this box if one or more numbers is self-corrected.
   - 2 = At least one of the following is present.
     - ☐ Only six to 11 correct numbers are present.
     - ☐ One or more numbers higher than the number 12 is present in addition to six to 12 correct numbers.
     - ☐ Six to 12 correct numbers are present, with one or more numbers perseverated.
   - 1 = Only one to five correct numbers are present.
   - 0 = No correct numbers are present.
2. Does the clock show 12 and only 12 of something? 1 0
   - 1 = The clock is divided by 12 of something (e.g., numbers, hands, dots).
   - 0 = One of the following is present.
     - ☐ The clock is divided by less than 12 of something.
     - ☐ The clock is divided by more than 12 of something (e.g., perseveration, extra numbers).
3. Are the numbers oriented correctly for reading vs. rotated? 1 0
   - 1 = Zero to two numbers are rotated.
   - 0 = Three or more numbers are rotated.
4. Are the numbers spaced correctly? 1 0
   - 1 = The numbers 12, 3, 6, and 9 are in the correct places, and other numbers are reasonably well spaced.
     - ☐ Check this box if placement/spacing of numbers is self-corrected.
   - 0 = Numbers are poorly placed/spaced.
5. Are the numbers inside the circle and arranged in a circular pattern? 1 0
   - 1 = Numbers are arranged in a circular pattern inside the circle. One or two numbers may stray from a circular pattern, but no number or less than half of any number is placed outside the circle.
   - 0 = At least one of the following is present.
     - ☐ No circular arrangement of numbers is evident.
     - ☐ Three or more numbers stray from a circular pattern.
     - ☐ At least half of one or more numbers is placed outside the circle.
     - ☐ One or more numbers is placed outside the circle.

Subscore 1

Clock Drawing, *continued*

Score

6. Are the numbers presented clockwise? 1 0
   - 1 = All numbers written are clockwise around the clock.
   - 0 = At least one of the following is present.
     - ☐ Numbers are counterclockwise.
     - ☐ Numbers are in a random arrangement.
     - ☐ Numbers are in columns.
7. How many hands are there? 1 0
   - 1 = Two hands are present.
   - 0 = One of the following is present.
     - ☐ No hands are present.
     - ☐ Only one hand is present.
     - ☐ More than two hands are present. (No penalty for a "seconds" hand.)
8. What lengths are the hands? 1 0
   - 1 = A distinguishable long hand and short hand are present.
     - ☐ Check this box if hand length is self-corrected.
   - 0 = One of the following is present.
     - ☐ Equal size hands are present.
     - ☐ No hands are present.
     - ☐ Only one hand is present.
     - ☐ More than two hands are present. (No penalty for a "seconds" hand.)
9. Where do the hands originate? 0
   - 1 = Hands (or a single hand if only one hand is present) emanate from the center of the circle, or within ½ inch from the center of the circle. Hands (if more than a single hand) touch, or come within ½ inch of touching at the point of origin.
   - 0 = At least one of the following is present.
     - ☐ Hands originate more than ½ inch from the center.
     - ☐ Hands are separated by more than ½ inch at the point of origin.
     - ☐ No hands are present.
10. Where do the hands point? 1 0
    - 1 = One hand is pointing to 11 and the other hand is pointing to 2, or one two-directional hand is pointing to 11 and 2.
      - ☐ Check this box if hand placement is self-corrected.
    - 0 = At least one of the following is present.
      - ☐ One or more hands is not pointing to 11 or 2.
      - ☐ No hands are present.
      - ☐ More than two hands are present. (No penalty for a "seconds" hand.)
11. Do the hands tell the correct time? 1 0
    - 1 = The short hand points to 11 and the long hand points to 2.
    - 0 = At least one of the following is present.
      - ☐ One or more hands does not point to the correct number.
      - ☐ Equal size hands are present.
      - ☐ No hands are present.
      - ☐ Only one hand is present.
      - ☐ More than two hands are present. (No penalty for a "seconds" hand.)

Subscore 2

Subscore 1

Clinician's Note

Clock Drawing serves as a mini-screening tool for all cognitive domains. This task can be readministered to sample and monitor examinees' progress, deterioration, or stability across several cognitive domains. Watch carefully as examinees draw the clock and note the strategies used. See Chapters 2 and 3 in the *Examiner's Manual* for information on scoring and analyzing visuospatial, planning, number, and time concept deficits.

Story Retelling

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	N/A	None	Provide as needed for initiation and completion.	You may repeat directions 1 time. Do not repeat the story.	2 minutes

Directions: Say, **"I'm going to tell you a short story. Listen carefully. I want you to repeat the whole story back to me *exactly* as I tell it to you. I can only read it one time. Are you ready?** (Repeat the directions if necessary.) **Okay, here it is."** Use a natural tone when reading the story.

> **Anna's husband gave her a beautiful ruby ring for her birthday. That night she decided to wear the ring but she couldn't find it. Anna searched everywhere and then began to cry. She reached into her pocket for her handkerchief and there was the ring.**

Say, **"Now, tell me the same story. Start now."** Start timing.

Prompts: If the examinee doesn't initiate the story, say, **"What was the story about? What happened?"** If the examinee tells an incomplete story before 2 minutes lapse, say, **"Anything else? Tell me more."**

Recording and Scoring: Place a check in the ✓ column for each targeted word or phrase (in bold print) or acceptable variation the examinee provides. Record verbatim any different responses. Score each check as 1 point. Check UN if a response is unintelligible.

Story Elements	✓	Acceptable Variations	UN	Response (if different)
1. Anna's				
2. husband				
3. gave her a		(got, bought, was given, received)		
4. beautiful		(pretty)		
5. ruby		(ruby red)		
6. ring				
7. for her birthday.				
8. That night she decided		(In the evening, one night)		
9. to wear the ring		(put it on, went to put the ring on)		
10. but		(however, and, then)		
11. she couldn't find it.		(discovered she lost it, the ring was gone, missing, misplaced)		
12. Anna		(She)		
13. searched		(looked, tried to find it, began looking, went to look)		
14. everywhere		(all over)		
15. and then began to cry.		(began to sob, bawl, started crying, got upset)		
16. She reached into her pocket				
17. for her handkerchief		(hankie, Kleenex®, tissue)		
18. and there was the ring.		(there it was, she found it, she pulled out a ring, it came out, she discovered it)		

Subscore 1 Max = 18

Clinician's Note

Story Retelling helps to assess auditory memory and comprehension, working memory, and language output skills. Unrelated responses may indicate loss of topic or memory problems. If partially correct information is provided, note whether recall is better for initial, medial, or final parts of the story as indications of arousal, attention, and storage capacity. Story Retelling is an easy way to assess narrative skills. Although no points are deducted for retelling the story out of sequence, you can analyze for recall of consecutive events building to the story conclusion by numbering each story element in the order reported.

Auditory Comprehension

Directions: Say, **"Now I'm going to ask some questions about the story. Just answer 'yes' or 'no.'"** Read the questions in order.

Recording and Scoring: Circle Y for yes or N for no. The correct response is in **bold type.**

Questions	Item 1	Item 2	Item 3
1. Was the woman's name Alice?	Y **N**		
2. Did her husband give her a ruby ring for her birthday?		**Y** N	
3. Did she accidentally throw her present away?			Y **N**
4. Was the woman's name Anna?	**Y** N		
5. Did her husband give her a diamond ring for her birthday?		Y **N**	
6. Did she find her present in her pocket?			**Y** N
Circle 1 for each column with both responses correct. Circle 0 for each column with only one or no responses correct.	Score 1 0	Score 1 0	Score 1 0

+ Subscore 1

= Subscore Total

Subscore Total	Story Retelling Score
0	0
1–2	1
3	2
4	3
5–6	4
7–8	5
9–10	6
11–12	7
13–14	8
15–16	9
17–18	10

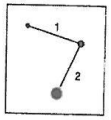
Story Retelling Score Max = 10

Symbol Trails

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Pages 5–10	Pen for examinee, Symbol Trails Scoring Transparency	Point to the first symbol on pages 6 and 10 if necessary.	You may repeat the directions 1 time.	Trial 1 = 2 min. Trial 2 = 2 min. Scored Item = 3 min.

Trial 1: Circles by Size

Directions: Place page 5 of the *Response Booklet* in front of the examinee. Say, **"Look at these circles. They are different sizes. I will connect them by drawing lines between them. I will start with the smallest circle and draw a line to the next biggest circle.** (Draw the first line as directed at right.) **Now I will draw a line to the biggest circle."** Draw the second line.

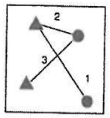


Turn to page 6 and say, **"That's what I want you to do on this page. Which is the smallest circle?** (Correct an incorrect choice of smallest circle by pointing to the correct circle.) **All right, now draw a line from that circle to the next biggest circle, and then keep going."** Provide the examinee with a pen.

Prompts: If the examinee asks for help, repeat the directions. If the examinee asks for additional help, say, **"I'm not allowed to help you. Just do the best you can."** If the examinee is still working after 2 minutes, say, **"Okay, time is up,"** or **"It's time to stop,"** and take the pen.

Trial 2: Alternating Shapes

Directions: Place page 7 of the *Response Booklet* in front of the examinee. Say, **"Now look at these circles and triangles. I will connect them by drawing lines between them. I will start with this circle and draw a line to a triangle.** (Draw the first line as directed at right.) **Now I will draw a line from the triangle to the other circle.** (Draw the second line.) **Now I will draw a line to the last triangle."** Draw the third line.



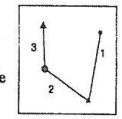
Turn to page 8 and say, **"That's what I want you to do on this page. Start with this circle.** (Point to the circle near the center of the page.) **Draw a line from this circle to a triangle, and then keep going, circle to triangle to circle, and so on."** Provide the examinee with a pen.

Prompts: If the examinee asks for help, repeat the directions. If the examinee asks for additional help, say, **"I'm not allowed to help you. Just do the best you can."** If the examinee is still working after 2 minutes, say, **"Okay, time is up,"** or **"It's time to stop,"** and take the pen.

Symbol Trails, *continued*

Scored Item: Alternating Sizes and Shapes

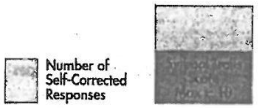
Directions: Place page 9 of the *Response Booklet* in front of the examinee. Say, **"Look at these circles and triangles. They are different sizes. I will connect them by drawing lines between them. I will start with the smallest circle and draw a line to the smallest triangle.** (Draw the first line as directed at right.) **Now I will draw a line to the next biggest circle, and then to the next biggest triangle."** Draw the second and third lines.



Turn to page 10 and say, **"That's what I want you to do on this page. Now, point to the smallest circle.** (Correct an incorrect choice of smallest circle by pointing to the correct circle.) **All right, draw a line from that circle to the smallest triangle and then keep going...circle, triangle, circle, and so on."** Provide the examinee with a pen.

Prompts: If the examinee asks for help, repeat the directions. If the examinee asks for additional help, say, **"I'm not allowed to help you. Just do the best you can."** If the examinee is still working after 3 minutes, say, **"Okay, time is up,"** or **"It's time to stop,"** and take the pen.

Recording and Scoring: Place the Symbol Trails Scoring Transparency over page 10 of the *Response Booklet*. Score 1 point for each correct or self-corrected line.



Clinician's Note

Symbol Trails is a nonlinguistic task used to help assess planning, self-monitoring, working memory, and visual attention even in examinees with compromised language skills. The two trial items introduce the concepts of graduating size and then alternating shapes. Examinees are required to manipulate both concepts in the Scored Item. As you observe examinees perform the task, check to see whether there is inattention to one side or quadrant of space and/or impulsivity. Note whether examinees self-monitor and correct errors.

Generative Naming

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit*
Pages 11 & 13	N/A	None	Prompt to encourage task completion.	You may repeat directions 1 time.	1 minute

Subtask 1—Animals

Directions: Turn to page 11 in the *Stimulus Manual* and show the word *animals* to the examinee. Say, **"I want you to name as many different animals as you can in 1 minute.** (Remove the *Stimulus Manual*.) **What animals can you think of?"** Start timing.

Prompts: If the examinee does not respond within 10 seconds, repeat the directions stressing the word *animals*. If the examinee asks if he or she already named a specific animal, say, **"I'm not allowed to help you. Just do the best you can."** If the examinee stops before the minute is up, you may prompt him or her by saying, **"Keep going; you have more time."**

Recording and Scoring: Write the responses in the spaces provided according to the four 15-second increments listed. For each response, place a check (✓) in the appropriate column to indicate Correct Responses (C), Perseverated Responses (P), or Other Types of Incorrect Responses (I). Total the number of responses in each column. Calculate the total number of C, P, and I responses and place the sums in the appropriate boxes in the lower right corner. Add C1, P1, and I1 to get the Total Number of Responses. Transfer the C1 Score to the appropriate box in Step 1 on page 12.

Animals

0–15 seconds	C	P	I	16–30 seconds	C	P	I	31–45 seconds	C	P	I	46–60 seconds	C	P	I
1.				1.				1.				1.			
2.				2.				2.				2.			
3.				3.				3.				3.			
4.				4.				4.				4.			
5.				5.				5.				5.			
6.				6.				6.				6.			
7.				7.				7.				7.			
8.				8.				8.				8.			
9.				9.				9.				9.			
10.				10.				10.				10.			
		P	I			P	I			P	I			P	I

= C1 + = P1 + = I1

Perseverated Responses (P1) ÷ Total Number of Responses = Perseveration Ratio =

Clinician's Note

In addition to quantifying word search and retrieval skills by one superordinate semantic category (Animals) and one phonetic category (*m* Words), the Generative Naming task enables you to qualitatively assess performance. Observe if examinees subcategorize animals (e.g., farm, zoo, pets) to aid word retrieval.

Perseveration Ratio: A ratio of 0.08 or greater indicates notable perseveration, which is indicative of brain damage. Example: 3 perseverations divided by 13 total Animals responses = 0.23 (notable perseveration). Abnormal perseveration ratios may have diagnostic value for mild/borderline dementia.

Is the Perseveration Ratio greater than or equal to 0.08? Yes ☐ No ☐

Generative Naming, *continued*

Subtask 2—*m* Words

Directions: Turn to page 13 in the *Stimulus Manual* and show the letter *m* to the examinee. Say, **"Now I want you to name as many words as you can that start with the letter *m*. Here are the rules. Do not name words that begin with a capital *m*. Do not say the same word again with a different ending, like *mop*, then *mopped* or *mopping*."** Remove the *Stimulus Manual*.

Say, **"Okay, you have 1 minute to name as many words you can think of that start with the letter *m*."** Start timing.

Prompts: If the examinee asks if he or she already named a specific word, say, **"I'm not allowed to help you. Just do the best you can."** If the examinee stops before the minute is up, you may prompt him or her by saying, **"Keep going; you have more time."**

Recording and Scoring: Write the responses in the space provided according to the four 15-second increments listed. Place a check (✓) in the appropriate columns to indicate Correct Responses (C), Perseverated Responses (P), or Other Types of Incorrect Responses (I). Total the numbers in each column. Calculate the total number of C, P, and I responses and place the sums in the appropriate boxes in the lower right corner.

m Words

0–15 seconds	C	P	I	16–30 seconds	C	P	I	31–45 seconds	C	P	I	46–60 seconds	C	P	I
1.				1.				1.				1.			
2.				2.				2.				2.			
3.				3.				3.				3.			
4.				4.				4.				4.			
5.				5.				5.				5.			
6.				6.				6.				6.			
7.				7.				7.				7.			
8.				8.				8.				8.			
9.				9.				9.				9.			
10.				10.				10.				10.			
		P	I			P	I			P	I			P	I

= C2 + = P2 + = I2

To determine the Generative Naming Score:

Step 1: Add the Correct Animals and *m* Words

Correct Animals (C1) + Correct *m* Words (C2) = Correct Animals + *m* Words =

Step 2: Use the table below to find the Generative Naming Score.

Correct Animals + *m* Words	Generative Naming Score
0	0
1–5	1
6–10	2
11–15	3
16–20	4
21–25	5
26–30	6
31–35	7
36–40	8
41+	9

Generative Naming Score Map = ?

Clinician's Note

Note "quick decay" (decreasing number of responses over the 15-second segments) or "slow rise" (increasing numbers of responses in later 15-second segments) during the Animals and *m* Words subtasks. Note whether examinees fail to maintain task ("loss of set"). Observe if they have difficulty switching from animals to *m* words ("stuck in set"). See Chapter 3 in the *Examiner's Manual* for more information.

Design Memory

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
Pages 14–19	N/A	None	None	You may repeat directions 1 time.	Show stimulus for 20 seconds. Allow 10 seconds for response to each task.

Item 1

Directions: Place page 14 of the *Stimulus Manual* in front of the examinee, so the designs are presented vertically. Say, **"Look at these designs carefully. I want you to remember what they look like. Try to remember them because I can only show them once."** After 20 seconds, turn the page. Present page 15 of the *Stimulus Manual* and say, **"Point to the designs I just showed you."**

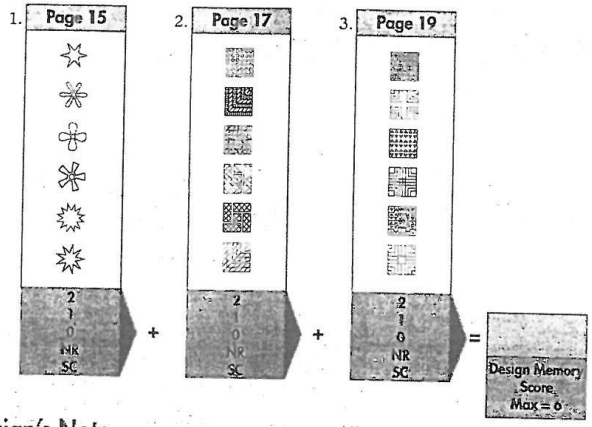
Item 2

Directions: Present page 16 and say, **"Look at these carefully. Try to remember them."** Wait 20 seconds, then turn to page 17. **"Point to the designs I just showed you."**

Item 3

Directions: Present page 18 and say, **"Look at these carefully. Try to remember them."** Wait 20 seconds, then turn to page 19. **"Point to the designs I just showed you."**

Recording and Scoring: Circle each design the examinee identifies. (Correct responses appear in **dark blue** below.) Score 1 point for each correct response. Circle NR if no response is given. Circle SC if the examinee self-corrects a response.



Clinician's Note

Design Memory is a nonlinguistic task that can provide information about visual discrimination and analysis, attention, and visual memory even in examinees with severe aphasia. Examinees with brain damage confined to the left hemisphere may perform normally, whereas those with right-hemisphere damage may perform poorly. This information can guide choice and use of treatment stimuli. In analyzing errors, look for impulsive choices and/or perseverations (e.g., pointing to designs in the same position across trials). See Chapter 3 in the *Examiner's Manual* for more information.

Mazes

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Pages 11 & 12	Pen for examinee	Prompt to encourage task completion.	You may repeat directions 1 time.	Maze 1 = 1 minute Maze 2 = 2 minutes

Maze 1

Directions: Open the *Response Booklet* to page 11 and place it in front of the examinee. Hand the examinee a pen. Point to the opening of the first maze, and say, **"Use the pen to trace a path through the maze to get to the money. Stay in the alleys and don't go through any walls. You have 60 seconds to complete the maze. Do you have any questions?** (Repeat directions if needed.) **Begin at the arrow.** (Point to the arrow.) **Start now."** Begin timing.

Maze 2

Directions: Turn to page 12 of the *Response Booklet*. Say, **"You have 2 minutes to trace a path through this maze. Do you have any questions?** (Repeat the directions if needed.) **Begin at the arrow.** (Point to the arrow.) **Start now."** Begin timing.

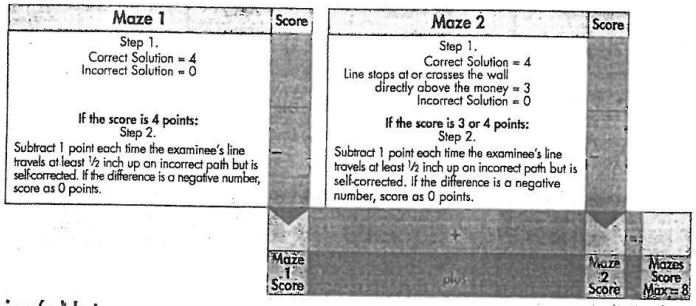
Prompts: Do not indicate to the examinee whether he or she is completing the maze correctly or give suggestions to assist him or her. If the examinee stops before completing the maze, you may prompt by saying, **"Keep trying. Just try to figure it out the best you can."**

Recording and Scoring: Score 4 points for a correct solution or 0 points for an incorrect solution for each maze. A solution is correct when the examinee's line begins at the arrow, follows the path, and ends at the money without crossing any walls. *See exception for Maze 2 below.**

Score 0 when at least one of the following occurs:

a. The examinee's line does not begin at the arrow.
b. The examinee's line crosses a wall.*
c. The examinee's line stops at any point before reaching the end/money.*
d. The examinee's line does not go through all the correct openings.*
e. The examinee's line traces a wall and does not follow the path.

*An exception is when the line stops at or crosses the wall directly above the money in Maze 2. In that case, deduct 1 point. See Chapter 2 in the *Examiner's Manual* for examples.



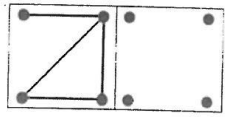
Clinician's Note

Satisfactory performance on this task requires planning, mental flexibility, self-monitoring, and visual discrimination. Poor planning and/or impulsivity will be reflected in lines going down incorrect paths and/or crossing walls. See Chapter 2 in the *Examiner's Manual* for scoring examples. Look for the ability to self-correct errors. Note neglect or inattention to one side of space. Compare performance on this task with that on the Symbol Trails task.

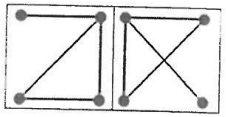
ign Generation

Stimulus Manual	Response Booklet	Additional Materials	Prompts	Repetitions	Time Limit
N/A	Page 13	Pen for examinee	Prompt once to use only four lines.	You may repeat directions 1 time.	3 minutes

Directions: Place page 13 of the *Response Booklet* in front of the examinee. Say, **"Here are four dots.** (Point to the dots in the left Demonstration Grid at the top of page 13.) **I'm going to connect the dots, using four lines to make a design."** Connect the dots as directed. The design should be oriented to the examinee as shown on the right.



"I used four lines to connect the four dots. I will make another design." Connect the dots on the right Demonstration Grid as directed at right.



"I made a different design using four lines. I want you to make as many different designs as possible, but don't copy my designs. Use four straight lines. (Point to the four lines on page 13.) **Make sure each line begins at a dot and ends at a dot.** (Point to dots midpage.) **You have 3 minutes. Remember to use four lines for each design. Start now."**

Prompt: If the examinee uses less or more than four lines to make a design, say, **"Use four lines and only four lines."** Only give the prompt once.

Recording and Scoring: Record the Total Number of Designs drawn by the examinee. Subtract from that number the different types of incorrect designs drawn by the examinee to get the Design Generation Score.

Scoring	Score
Total Number of Designs	
Number of Demonstration Designs That Were Copied (maximum of two designs)	–
Number of Perseverated Designs (any time an examinee's design is repeated, count it as a Perseverated Design)	–
Number of Designs With Greater or Less Than Four Lines	–
Other Types of Incorrect Designs	–
Number of Self-Corrected Designs	
Design Generation Score Max = 10	

Clinician's Note

This is a nonlinguistic task of creativity and mental flexibility. Look for perseverative responses, failure to maintain four straight lines connecting four dots, and/or neglect of stimuli on one side of space. Refer to Chapters 2 and 3 in the *Examiner's Manual* for examples of these and other error types.

Summary Scoring Worksheet

1. Transfer each task score from the appropriate page to the Cognitive Domain Score Table below.
2. Multiply each task score by the numbers specified across the row.
3. Add the multiplied numbers down each column to determine the examinee's score for each Cognitive Domain.

Cognitive Domain Score Table

Task	Criterion Cut Scores* 18–69	70–89	Score	Attention	Memory	Executive Functions	Language	Visuospatial Skills
Personal Facts, p. 2	8	8			x 7=		x 1=	
Symbol Cancellation, p. 3	11	10		x 9=				x 2=
Confrontation Naming, p. 4	10	10					x 1=	
Clock Drawing, p. 6	12	11						
Story Retelling, p. 8	6	5		x 2=	x 6=		x 1=	
Symbol Trails, p. 10	9	6		x 3=		x 1=		x 2=
Generative Naming, p. 12	5	4			x 1=	x 1=	x 1=	
Design Memory, p. 13	5	4		x 2=	x 10=			x 4=
Mazes, p. 14	7	4		x 4=		x 1=		x 3=
Design Generation, p. 15	6	5		x 1=		x 1=		x 1=
			Cognitive Domain Score =					

* If desired, check the examinee's performance on individual tasks by referring to the Criterion Cut Scores. If the score is at or above the Criterian Cut Score, performance is considered within normal limits for a task.

1. Choose the Severity Ratings Table appropriate for the examinee's age group. Transfer the examinee's Cognitive Domain Scores to the appropriate Severity Ratings Table.
2. Circle the Range of Severity that corresponds with the examinee's score for each domain.
3. Circle the Severity Rating that corresponds with the range circled for each cognitive domain.
4. Total the Severity Ratings. Divide by 5 to get the Composite Severity Rating.
5. Circle the appropriate Composite Severity Rating Range.
6. Transfer the severity ratings (WNL, Mild, etc.) for each domain and for the Composite Severity Rating Range to the Severity Ratings Summary on page 1.

Severity Ratings Table for Ages 18–69 Years

Cognitive Domain	Score	Ranges of Severity: WNL* 4	Mild 3	Moderate 2	Severe 1	Severity Rating
Attention		215–180	179–125	124–50	49–0	4 3 2 1
Memory		185–155	154–141	140–110	109–0	4 3 2 1
Executive Functions		40–24	23–20	19–16	15–0	4 3 2 1
Language		37–29	28–25	24–21	20–0	4 3 2 1
Visuospatial Skills		105–82	81–52	51–42	41–0	4 3 2 1
					Total	
					Divide by 5	
Composite Severity Rating =						

Severity Ratings Table for Ages 70–89 Years

Cognitive Domain	Score	Ranges of Severity: WNL* 4	Mild 3	Moderate 2	Severe 1	Severity Rating
Attention		215–160	159–100	99–40	39–0	4 3 2 1
Memory		185–141	140–115	114–80	79–0	4 3 2 1
Executive Functions		40–19	18–14	13–8	7–0	4 3 2 1
Language		37–28	27–25	24–16	15–0	4 3 2 1
Visuospatial Skills		105–62	61–37	36–22	21–0	4 3 2 1
					Total	
					Divide by 5	

Composite Severity Rating Range			
WNL*	Mild	Moderate	Severe
4.0–3.5	3.4–2.5	2.4–1.5	1.4–1.0

Composite Severity Rating =

1. Choose the Clock Drawing Severity Ratings Table appropriate for the examinee's age group. Transfer the examinee's Clock Drawing Score from page 6 to the appropriate table.
2. Circle the Range of Severity that corresponds with the examinee's Clock Drawing Score.
3. Transfer the Clock Drawing Severity Rating to the Severity Rating Summary on page 1.

Clock Drawing Severity Ratings for Ages 18–69 years

	Score	Ranges of Severity: WNL*	Mild	Moderate	Severe
Clock Drawing, p. 6		13–12	11–10	9–8	7–0

Clock Drawing Severity Ratings for Ages 70–89 years

	Score	Ranges of Severity: WNL*	Mild	Moderate	Severe
Clock Drawing, p. 6		13–11	10–9	8–7	6–0

*Within normal limits.

Appendix VI - Reliability and validity tables pertaining to the CLQT

Table: Test-Retest Means, Standard Deviations, Stability Coefficients, Standard Error of Measurements and Mean Absolute Score Differences for Each Task and Cognitive *Domain (n = 46)*

	1st Administratio		2nd Administration				Mean Absolute Score	Maxim
Task	**Mean**	***SO***	**Mean**	***SD***	**<-12[a]**	**SEM**	**Difference**	**Points**
Personal Facts	**8.00**	**0.00**	**8.00**	**0.00**	__		**0.00**	**8**
Symbol	**11.13**	**2.99**	**11.74**	**0.74**	**0.62**	**1.84**	**0.87**	**12**
Confrontation	**9.98**	**0.15**	**10.00**	**0.00**	—		**0.02**	**10**
Clock Drawing	**12.35**	**1.23**	**12.57**	**1.00**	**0.74**	**0.63**	**0.48**	**13**
Story Retelling	**8.33**	**1.43**	**8.61**	**1.20**	**0.62**	**0.88**	**0.89**	**10**
Symbol Trails	**9.15**	**1.78**	**9.43**	**1.28**	**0.14**	**1.65**	**1.02**	**10**
Generative	**6.61**	**1.74**	**6.39**	**1.76**	**0.81**	**0.76**	**0.83**	**9**
Design Memory	**5.72**	**0.58**	**5.72**	**0.46**	**0.03**	**0.57**	**0.39**	**6**
Mazes	**7.30**	**1.28**	**7.33**	**1.28**	**0.43**	**0.97**	**0.67**	**8**
Design Generation	**8.13**	**2.27**	**8.93**	**2.46**	**0.63**	**1.38**	**1.72**	**13**
Cognitive Domain								
Attention	**193.0**	**29.76**	**200.85**	**12.35**	**0.69**	**16.57**	**11.74**	**215**
Memory	**169.7**	**11.53**	**171.22**	**10.03**	**0.61**	**7.20**	**7.39**	**185**
Executive	**31.20**	**4.65**	**32.09**	**5.02**	**0.90**	**1.47**	**1.85**	**40**
Language	**32.91**	**2.67**	**33.00**	**2.57**	**0.81**	**1.16**	**1.22**	**37**
Visuospatial Skills	**93.48**	**9.99**	**96.13**	**7.33**	**0.71**	**5.38**	**5.26**	**105**

"Because the standard deviation was 0.00 on the second test administration, it was not possible to calculate a correlation coefficient.

[b]Difference Scores can be positive or negative. Taking the mean of both positive and negative scores yields a number misleadingly close to zero. Therefore, the absolute value of each score difference was taken and the mean absolute difference was calculated.

Table: CLQT Goodness-of-Fit Statistics for Confirmatory Factor Analyses

Domain	chi-squaredf		chi-square/df		NNFI	RMSEA	ECVI
Attention	**25.22**	**9**	**2.80**	**0.01**	**0.97**	**0.15**	**0.76**
Memory	**2.46**	**2**	**1.23**	**0.29**	**0.99**	**0.05**	**0.33**
Executive Functions	**3.06**	**2**	**1.53**	**0.21**	**0.99**	**0.08**	**0.33**
Language	**0.92**	**3**	**0.30**	**0.81**	**1.00**	**0.00**	**0.28**
Visuospatial Skills	**6.81**	**5**	**1.36**	**0.23**	**0.99**	**0.06**	**0.46**

Table: Comparison of a Matched Set of CLQT Nonclinical (n = 38) and Clinical (n = 38) Research Sample Task Means and Standard Deviations

Task		Sample		t
		Nonclinical	Clinical	
Personal Facts	Mean	7.97	6.37	4.24*
	SD	0.16	2.33	
Symbol Cancellation	Mean	11.05	7.79	3.55*
	SD	2.73	4.97	
Confrontation Naming	Mean	9.97	9.28	2.62*
	SD	0.16	1.63	
Clock Drawing	Mean	11.95	8.50	5.14*
	SD	1.71	3.77	
«				
Story Retelling	Mean	7.68	4.74	6.18*
	SD	1.51	2.52	
Symbol Trails	Mean	8.71	4.66	5.98*
	SD	2.34	3.47	
Generative Naming	Mean	6.00	2.92	8.45*
	SD	1.45	1.71	
Design Memory	Mean	5.42	3.97	6.30*
	SD	0.79	1.17	
Mazes	Mean	6.84	4.05	5.30*
	SD	1.62	2.81	
Design Generation	Mean	7.00	3.55	7.02*
	SD	2.09	2.19	

*(#=37, p< .01

Table: ***Comparison of a Matched Set ofCLQT Nonclinical (n = 38) and Clinical (n = 38) Research Sample Cognitive Domain Means and Standard Deviations***

		Sample		
Cognitive Domain		**Nonclinical**	**Clinical**	
Attention	Mean	186.18	121.26	5.73*
	SD	30.00	63.06	
Memory	Mean	162.13	115.66	7.27*
	SD	13.35	37.06	
Executive Functions	Mean	28.55	15.18	8.89*
	SD	5.04	7.78	
Language	Mean	31.63	23.30	7.12*
	SD	2.45	6.78	
Visuospatial Skills	Mean	88.74	56.50	6.90*
	SD	13.07	25.68	

*(#=37,p<.01

Appendix VII - Structured Interview Schedule

INTERVIEW SCHEDULE REGARDING THE IMPACT OF COGNITIVE-LINGUISTIC ABILITIES ON THE QUALITY OF LIFE OF PERSONS WITH HIV/AIDS.

PART ONE: INFORMATION FROM RECORD REVIEW AND INTERVIEW

Demographic Information, medical and psychological History:			
Date:		Number:	
Name Telephone #		Address	
Name of friend or Relative		Contact #	
CD4 count:		Age	
Gender		Date of Onset	
Time in months or years since diagnosis			
Education : Highest grade completed:		Present Occupation: Working	

What were your best subjects: What were your worst subjects: Did you need remedial help? Reasons for leaving High school? What other qualifications do you have ?		(How long) Job duties: Not working (How long) Previous occupation: Job duties:	
Marital Status? Married, single, divorced		Have you ever injured your head? How?	

Number of years married? Number and ages of Children?		Have you ever been hospitalised?	
Medication:			
Opportunistic Infections and related Medical Pathologies: E.g. Meningitis, encephalopathy, other			

PART TWO: INFORMATION FROM THE INTERVIEW PERTAINING TO COGNITION AND LANGUAGE:

Memory: Do you have difficulty remembering:	Yes	No
To take you medication on time		
To turn off the lights or stoves		
To lock the doors		
To pay bills, fees etc.		
Where you placed things e.g. keys		
Directions to a new place		
To keep appointments		
The day, month, year or time of day		
To arrive on time		

Things you do to remember.

- Do you rely on other people to help you remember?

- Do you write things down?

- Do you keep all the information in your head?

Attention: *<u>Internal Distractors:</u>* Do you experience:	*Yes*	*No*
feeling tired (describe)		
headaches (describe)		
pain (describe)		
dizziness		
Fear or scared		
anger (describe)		
sadness, depression, tearfulness (describe)		
Have you taken medicine for depression or other emotional problems? What was the cause?		
Have you ever thought of committing suicide?		
Do you worry about dying?		
Do you worry about finances?		
Do you worry about keeping your job?		
Do you worry about your children?		

External Distractors: Do you have difficulty:		
focusing if there's a lot of movement		
focusing on a task or person if more than one person is speaking		
focusing if the radio or tv is playing in the background		
Sustained Attention: Do you have difficulty:		
staying interested in a task for more than an hour		
staying focused on a telephone conversation		
staying focused on what the doctor or nurse says		
staying focused on complex information		
Do you find that you are easily distracted?		
Visual: Do you experience difficulty : Yes No		
Blurred vision		
Spots when you look at something		
Seeing objects that are not there		
Eye pain, headaches, vomiting, dizziness		
Bumping into objects/walls		
Seeing objects in a distance		
Executive functions: Do you have difficulty:		
Adding up or doing maths in your head		

Answering questions quickly		
Understanding what you hear the first time you hear it		
Making decisions		
Starting a task?		
Completing or finishing a task?		
Seeing your mistakes and correcting them?		
following directions?		
Solving a problem e.g. If you were lost what would you do? A least two solutions		
Language: ***Hearing:*** ***yes no***		
Have you ever had your hearing tested?		
Do you hear things only when they are loud?		
Do you have difficulty hearing a person when there is background noise?		
Do you experience nausea, dizziness, pain in the ear, ringing or buzzing?		
Expressive Language: Do you have difficulty:		
talking for a long period of time		
spelling words correctly		

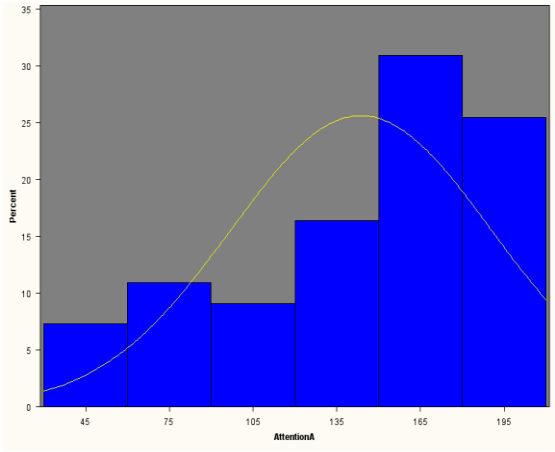
writing		
starting a conversation		
speaking on the telephone		
maintaining a conversation		
Do people finish your words for you?		
***Receptive language*:**		
Do you have to ask people to repeat themselves when talking to you?		
Do you have difficulty :		
remembering what someone has asked you		
remembering a telephone conversation		
understanding what the doctor or nurse said		
remembering information you have read (newspaper, magazine, book)		
understanding directions		
understanding jokes		
Impact of Cognitive and Language problems Do you feel nervous and anxious when you talk to people?	Yes	No
Do you feel like you are burden to your family? If so why?		
Does your diagnosis or other problems affect your job ?Describe		
Does your diagnosis or other problems affect your relationships with other people including family? Describe		

Do people act differently how people (family, friends, etc.) act around you? Describe		
Has your diagnosis or other problems affected you self-worth? Describe		
Does your diagnosis or other problems affect your social life i.e how you interact with people, places you visit etc?		
Are you able to cope with your problems (cognitive i.e. memory, attention etc. and language)? Describe how you are coping.		

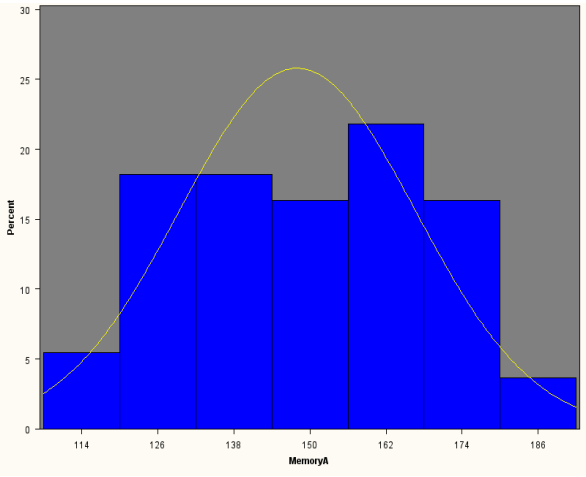
Thank You

Appendix VIII - Normality of data

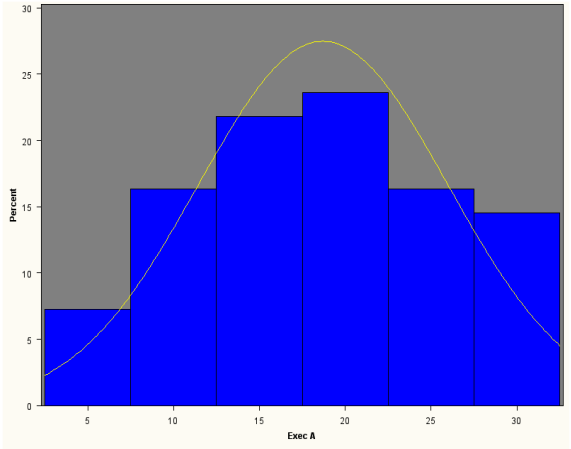
Experimental–CLQT-Baseline-Attention



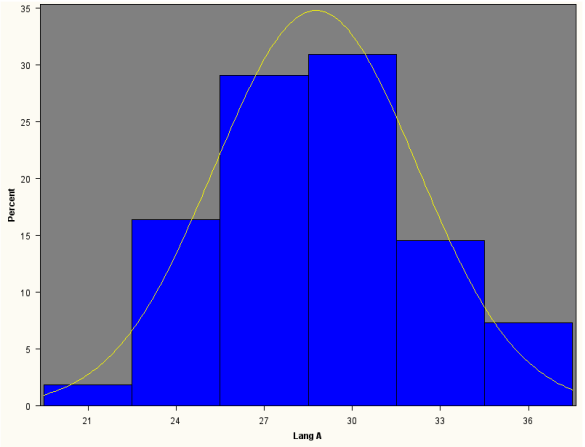
Experimental–CLQT-Baseline-Memory



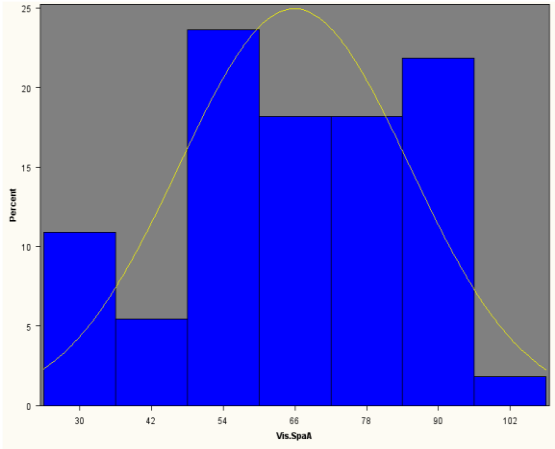
Experimental–CLQT-Baseline-Executive Function



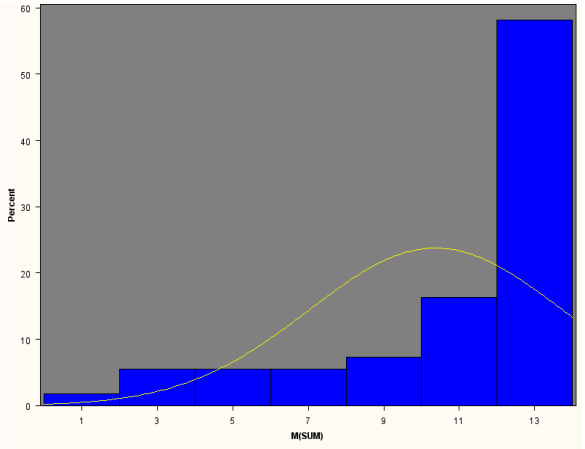
Experimental–CLQT-Baseline-Language



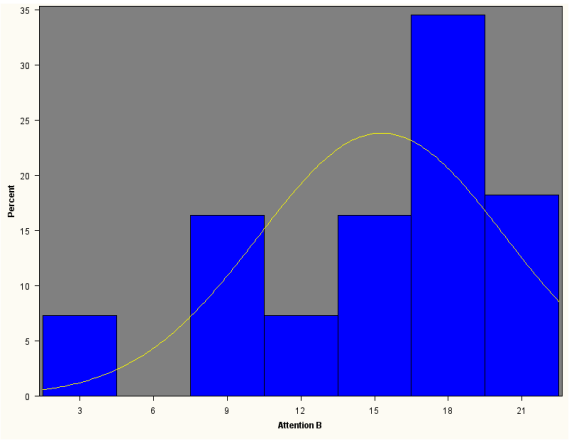
Experimental-CLQT–Baseline-Visual Spatial



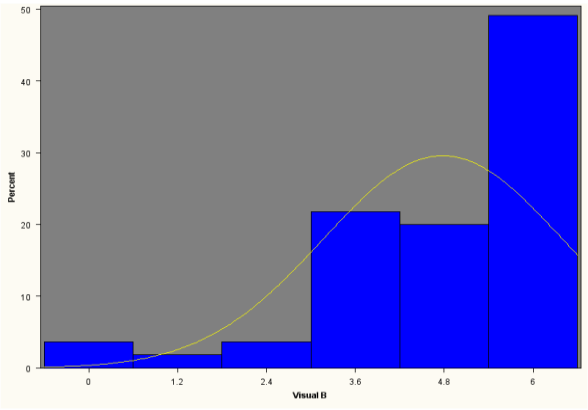
Experimental – IS-Baseline-Memory



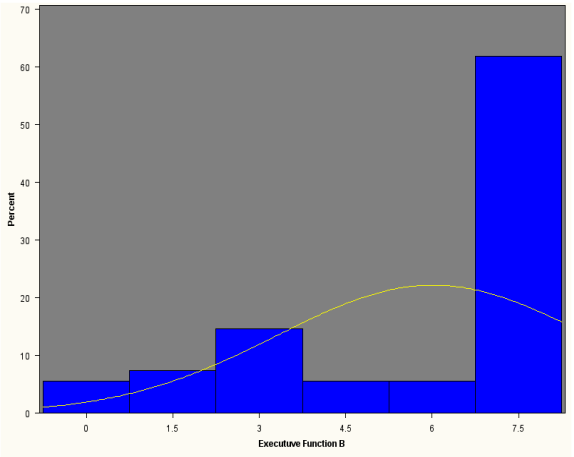
Experimental –IS–Baseline-Attention



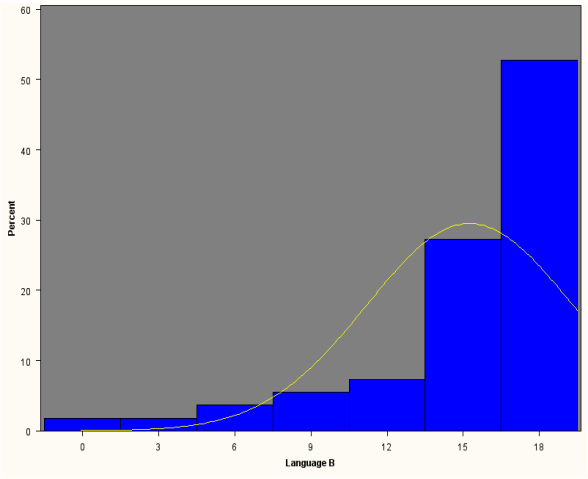
Experimental – IS–Baseline-Visual Spatial



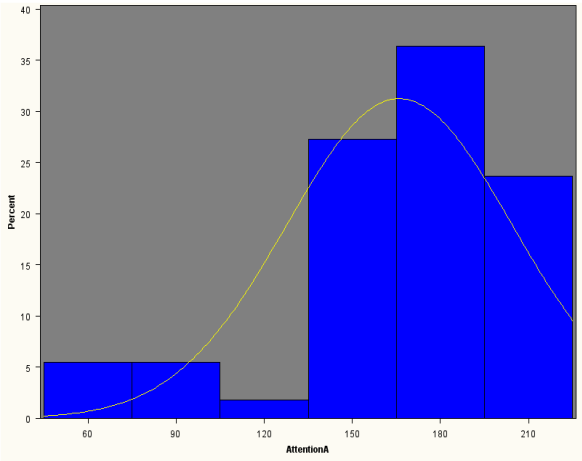
Experimental–IS–Baseline–Executive Function



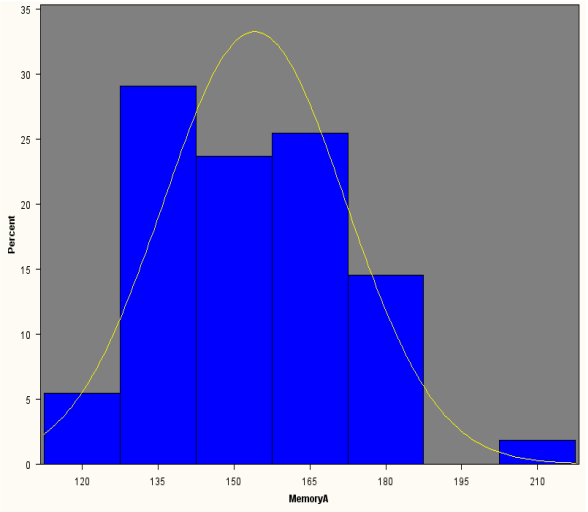
Experimental–IS–4 months -Language



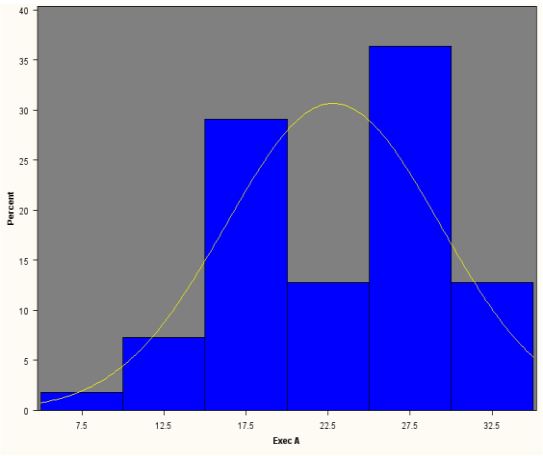
Experimental–CLQT-4months-Attention



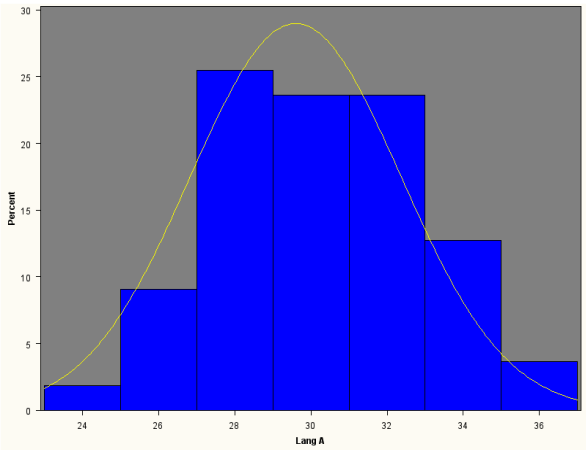
Experimental –CLQT–4 Months –Memo



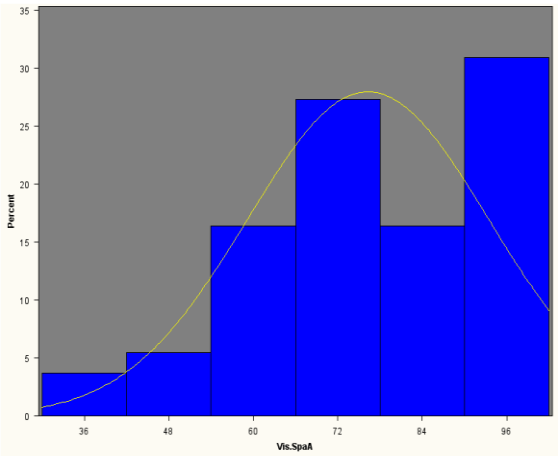
Experimental-CLQT-4months-Executive Function



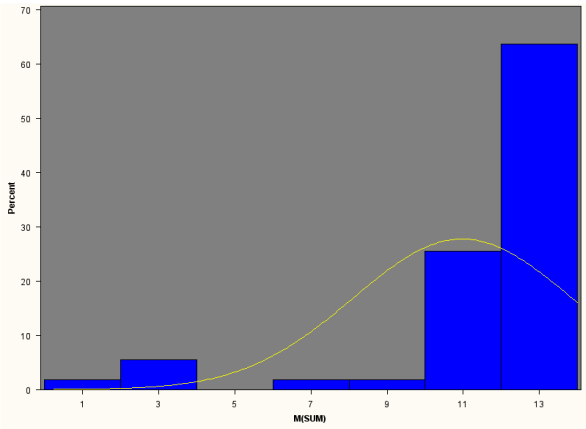
Experimental-CLQT-4months-Language



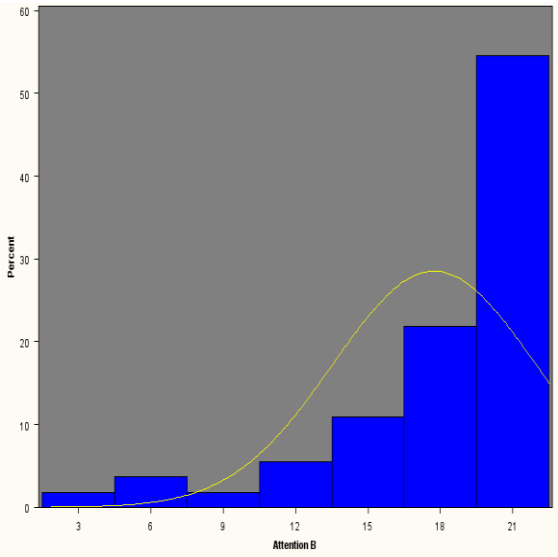
Experimental –CLQT–4 months – Visual Spatial



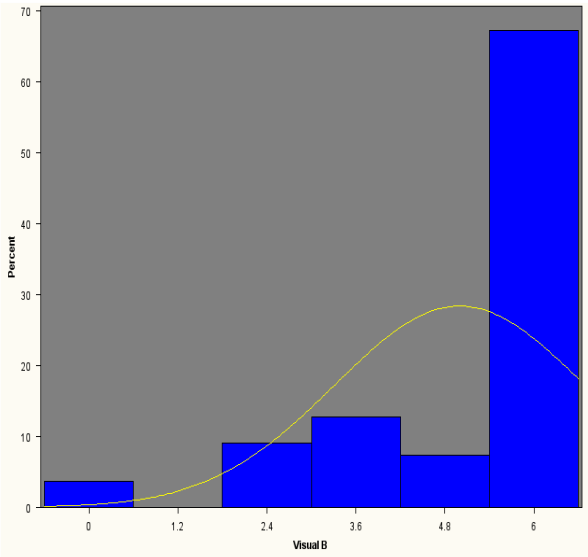
Experimental –IS-4 months-Memory



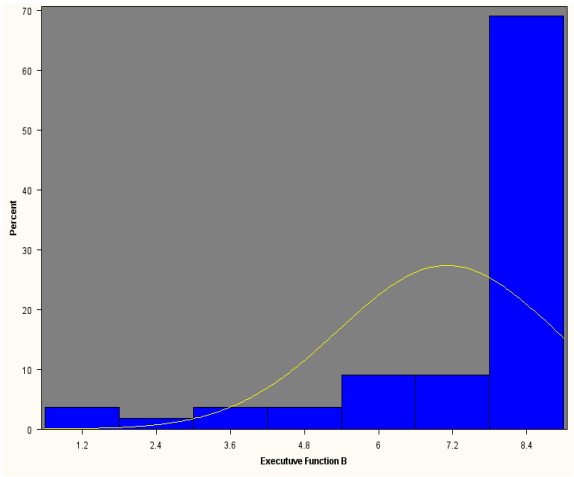
Exeperimental-IS-4months-Attention



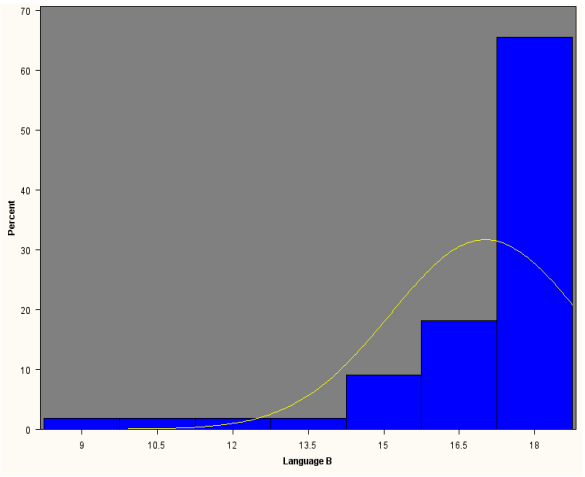
Experimental-IS-4months-Visual Spatial



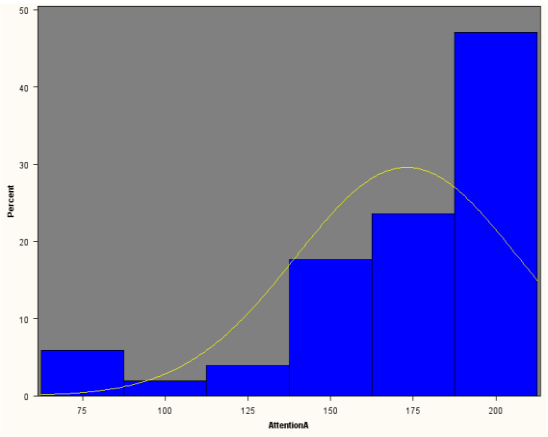
Experimental–IS–4 months–Executive Function



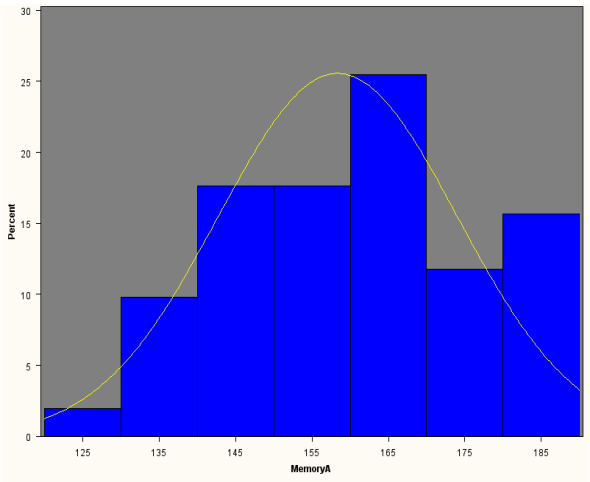
Experimental–IS–4 months -Language



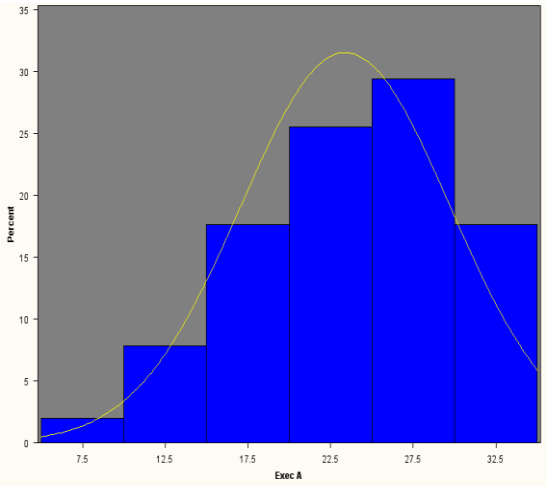
Experimental – CLQT-8 months-Attention



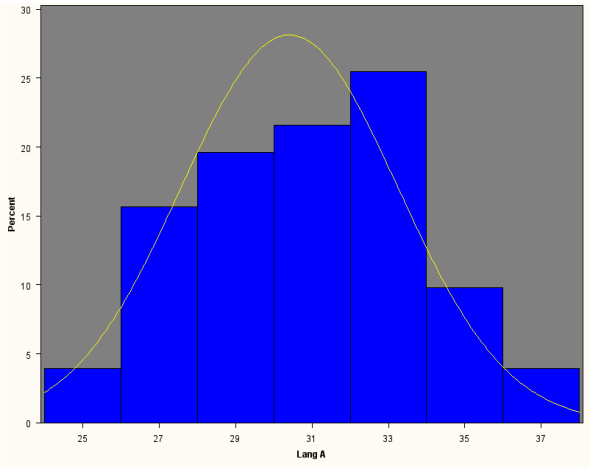
Experimental-CLQT-8months-Memory



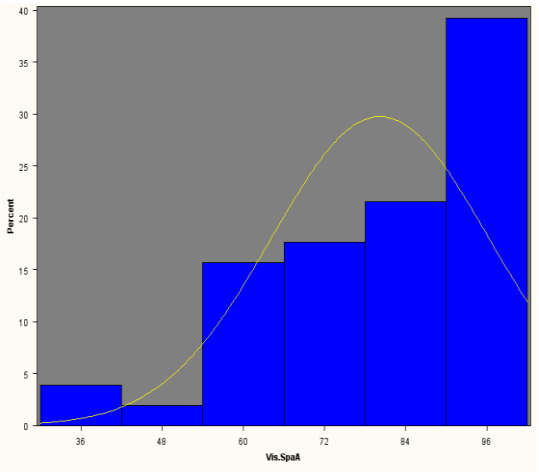
Experimental-CLQT-8months-Executive Function



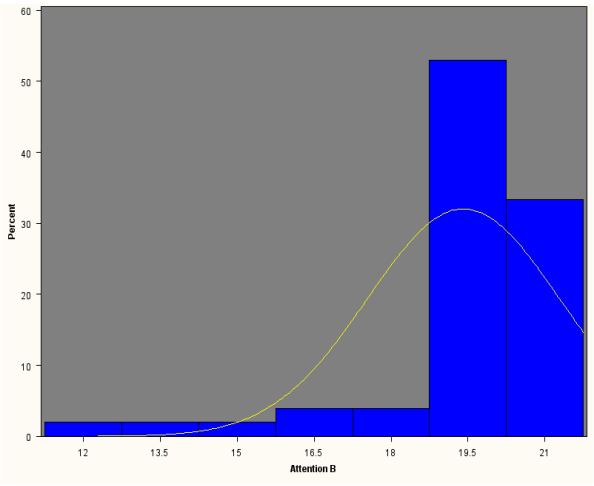
Experience-CLQT-8months-Langauage



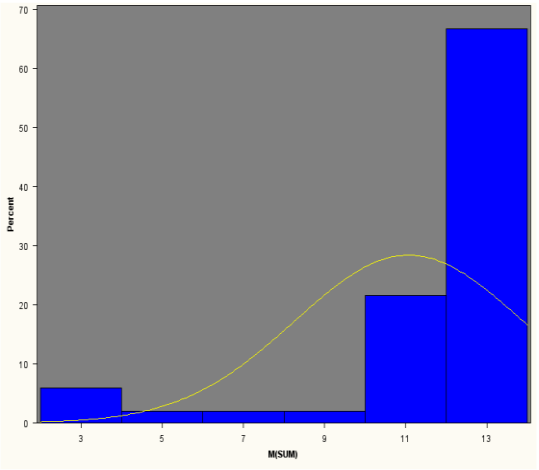
Experimental-CLQT-8months-Visual Spatial



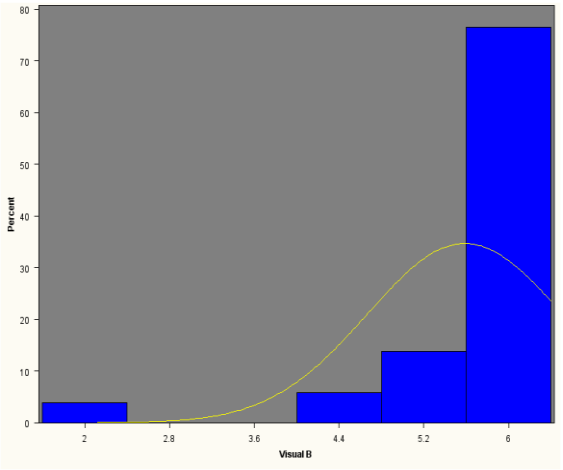
Experimental – IS- 8 months- Attention



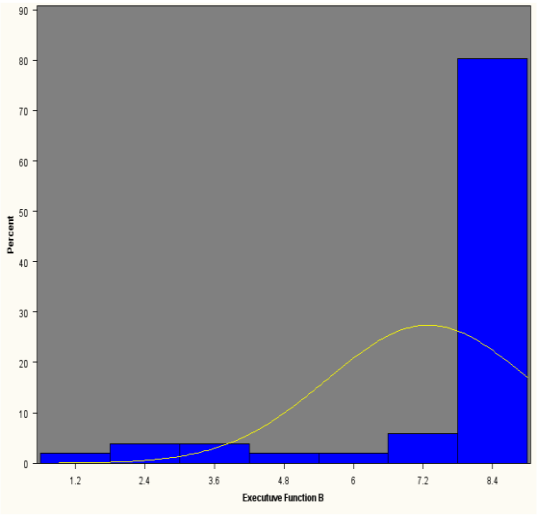
Experimental-IS- 8months-Memory



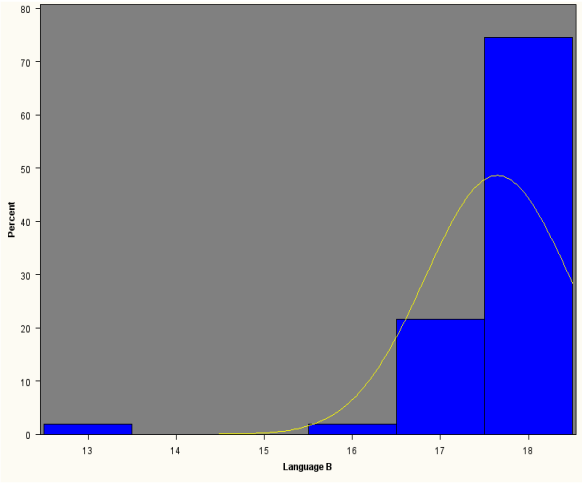
Experimental- IS- 8 months-Visual Spatial



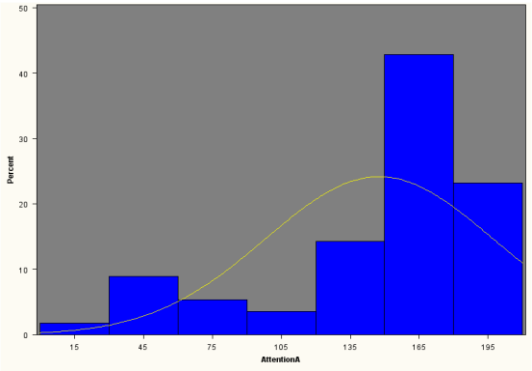
Experimental-IS-8months-Excecutive Function



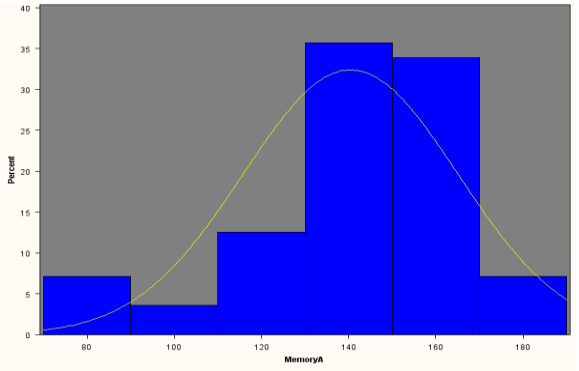
Experimental-IS-8months-Language



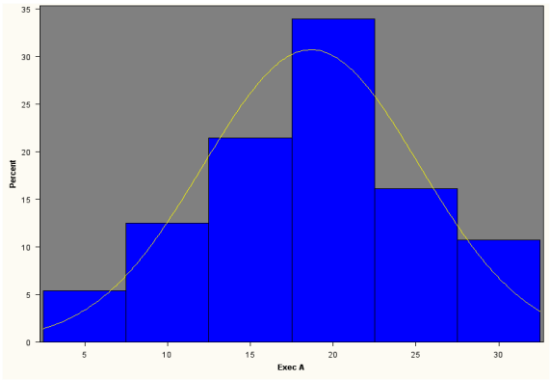
Cross Sectional–CLQT-Attention



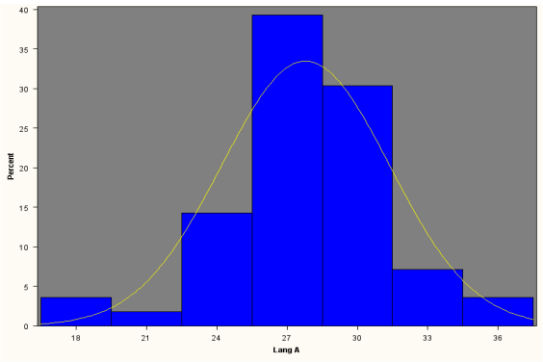
Cross Sectional- CLQT- Baseline-Memory



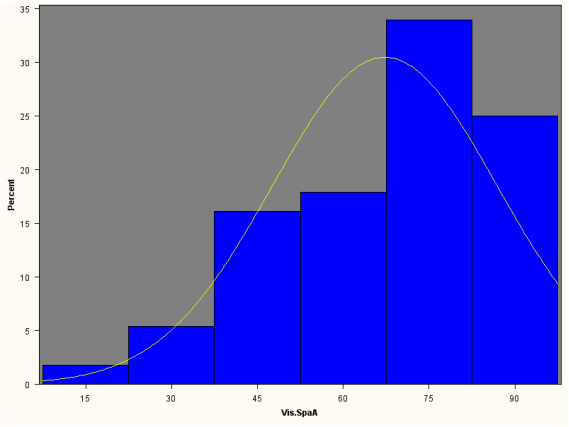
Cross Sectional – CLQT- Baseline-Executive Function



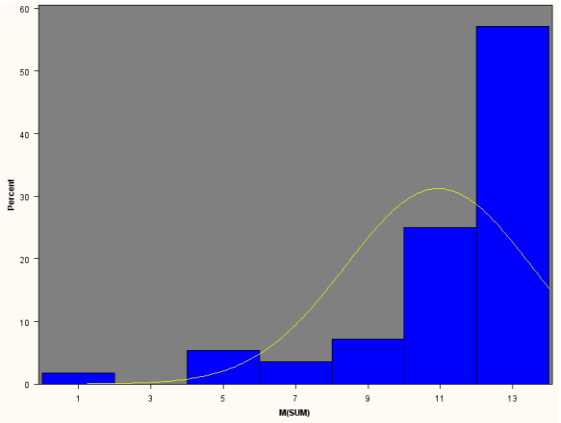
Cross Sectional- CLQT- Baseline-Language



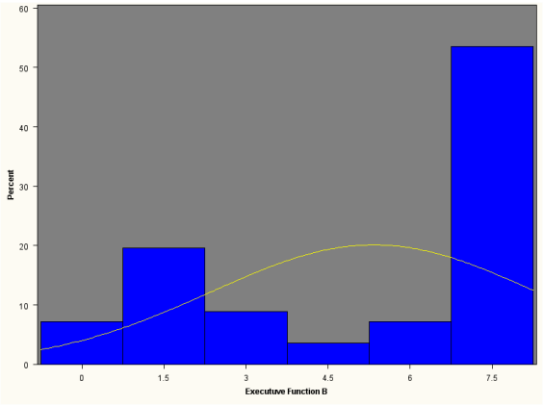
Cross Sectional- CLQT-Baseline-VS



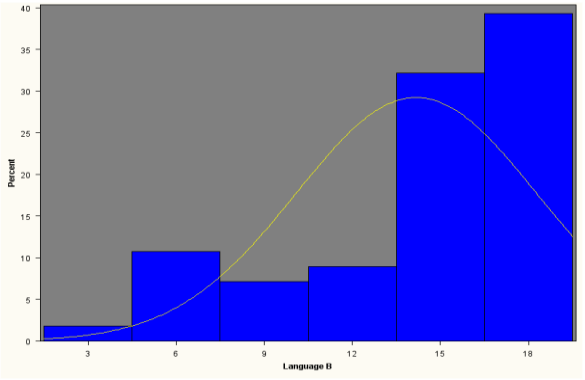
Cross sectional –IS- Baseline-Memory



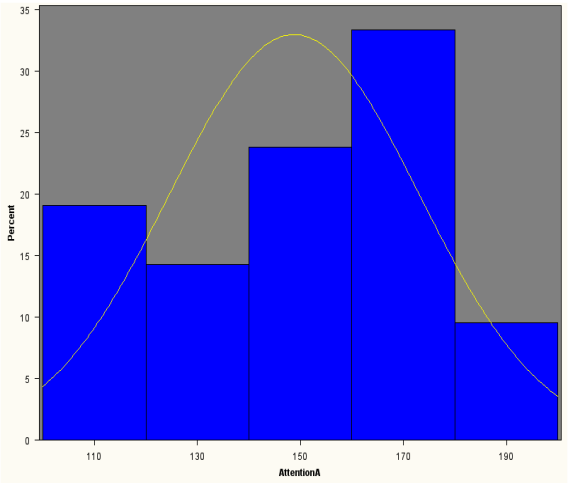
Cross Sectional- IS -Baseline-Executive Function



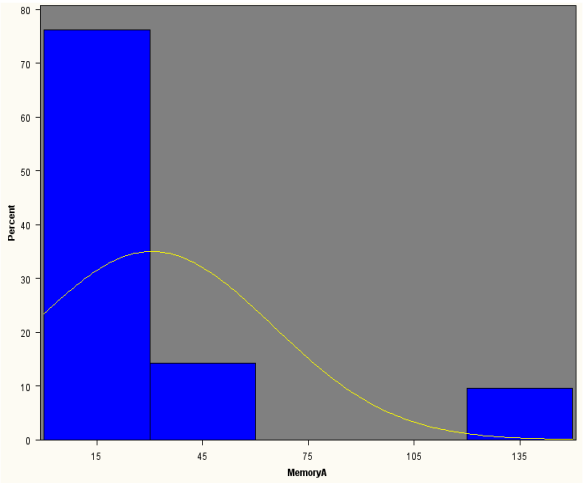
Cross Sectional- IS -Baseline- Language



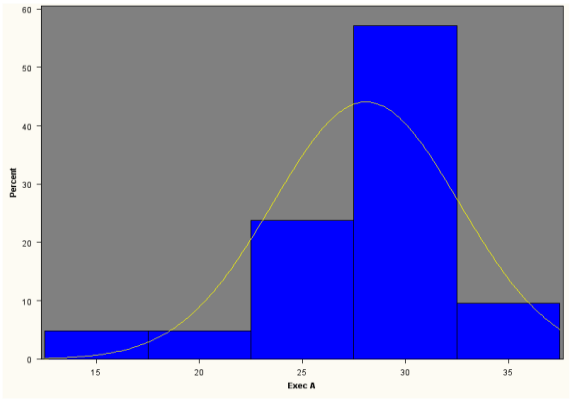
Comparison- CLQT -Baseline-Attention



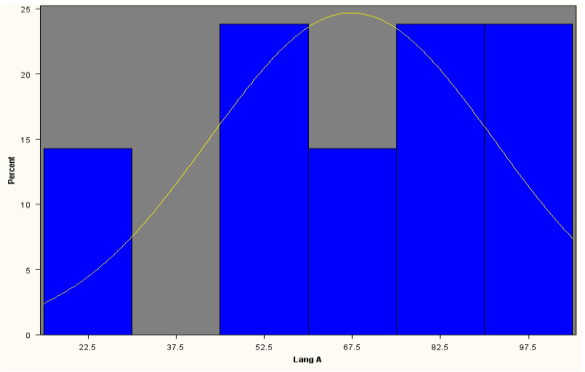
Comparison – CLQT- Baseline- Memory



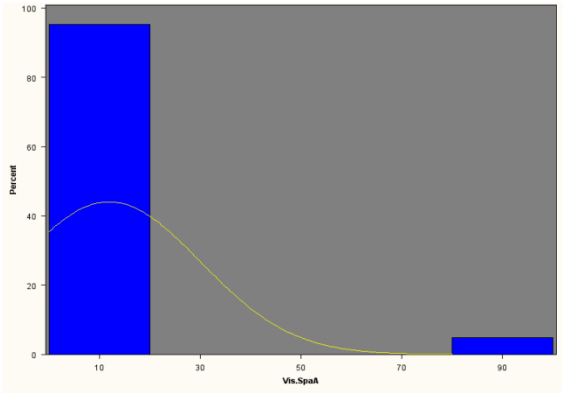
Comparison- CLQT -Baseline- Executive Function



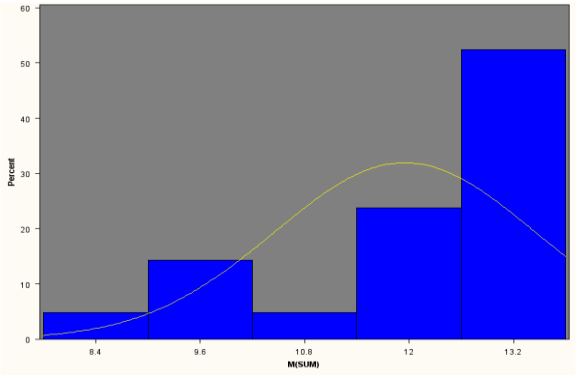
Comparison-CLQT -Baseline- Language



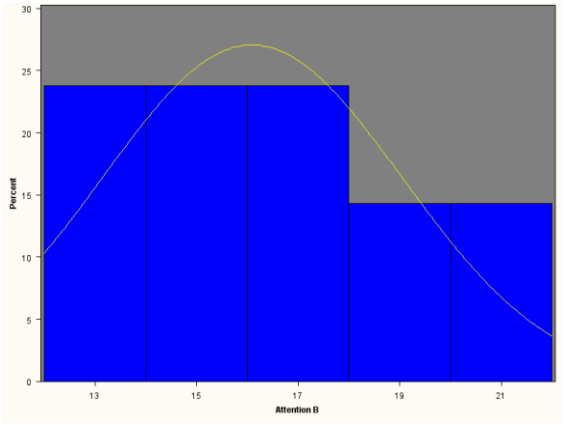
Comparison- CLQT- Baseline-Visual Spatial



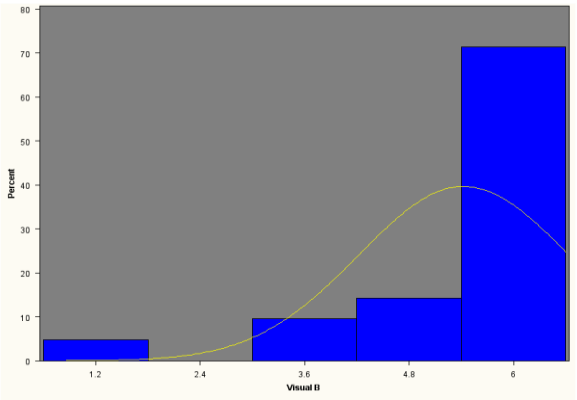
Comparison – IS- Baseline -Memory



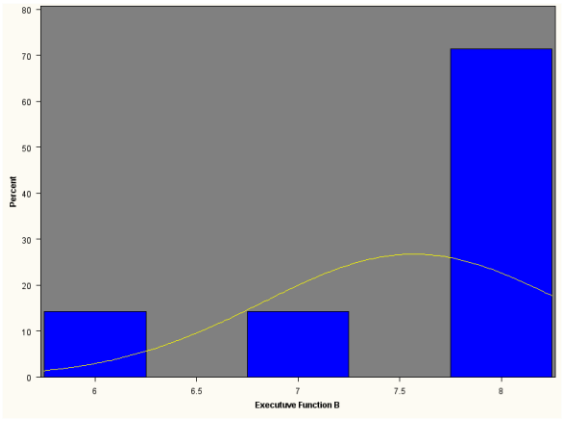
Comparison –IS -Baseline-Attention



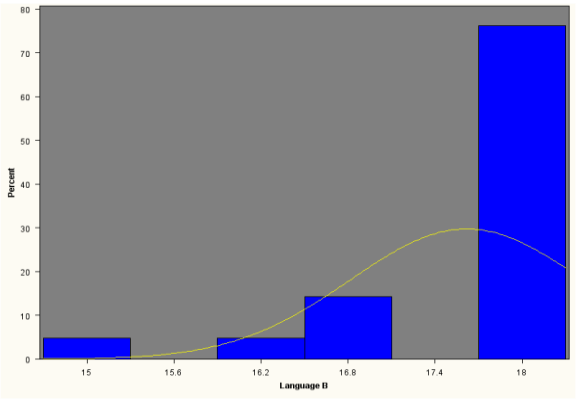
Comparison –IS Baseline-Visual Spatial



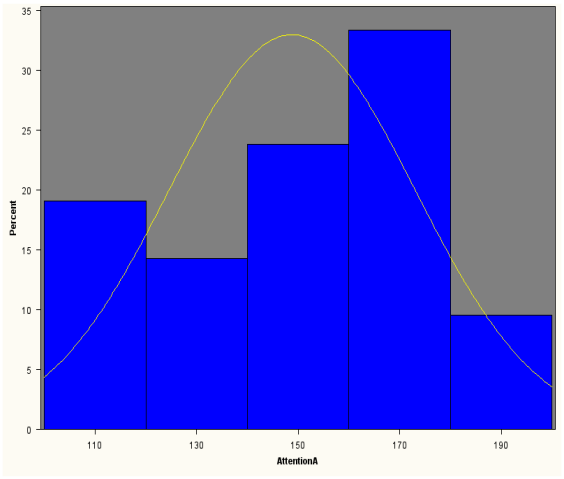
Comparison-IS-Baseline-Executive Function



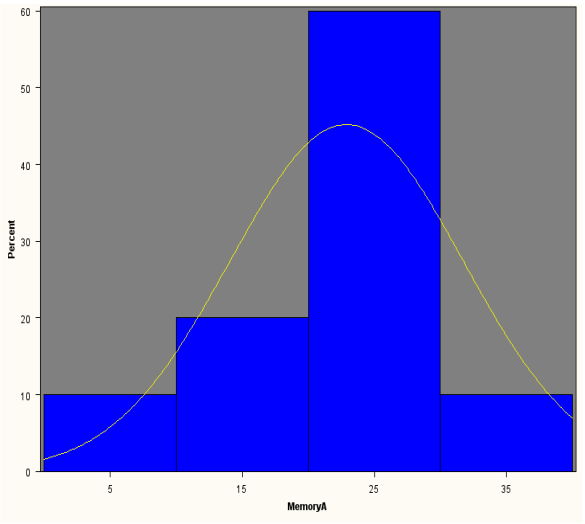
Comparison- IS-Baseline-Language



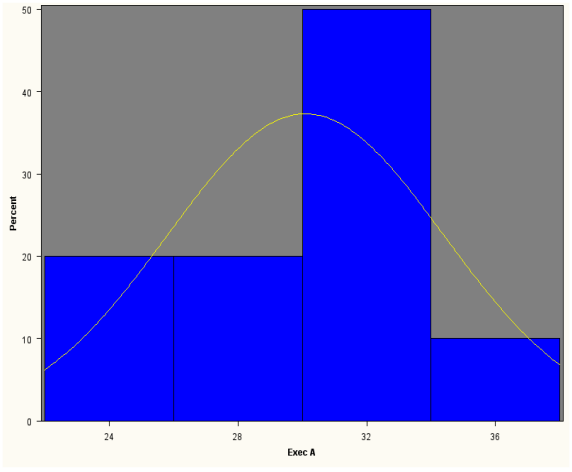
Comparison- CLQT-4 months-Attention



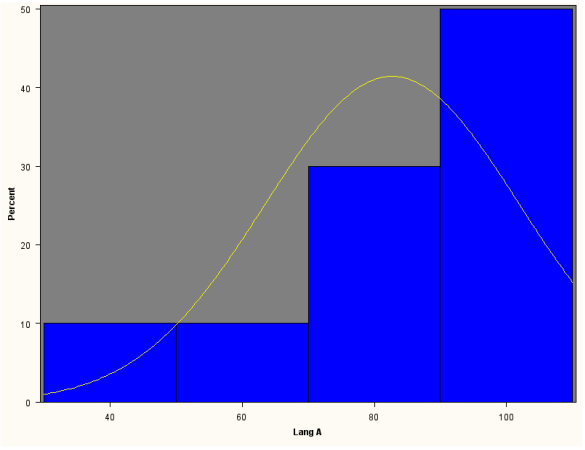
Comparison – CLQT-4 months-Memory



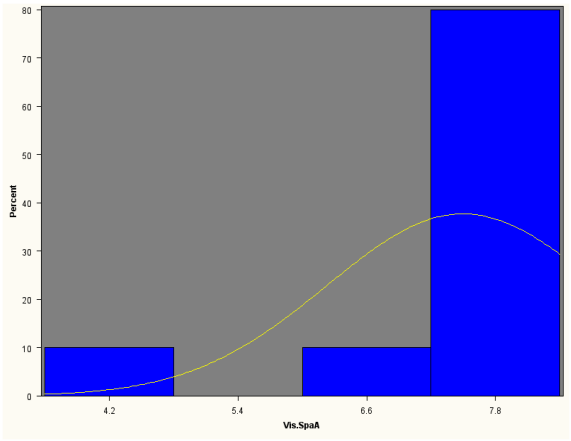
Comparison-CLQT-4 months-Executive Function



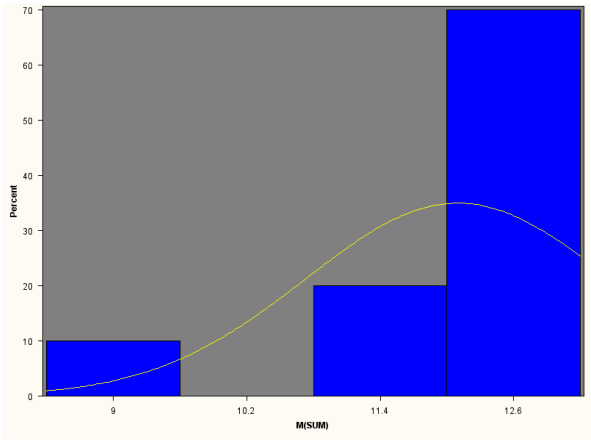
Comparison-CLQT-4 months-Language



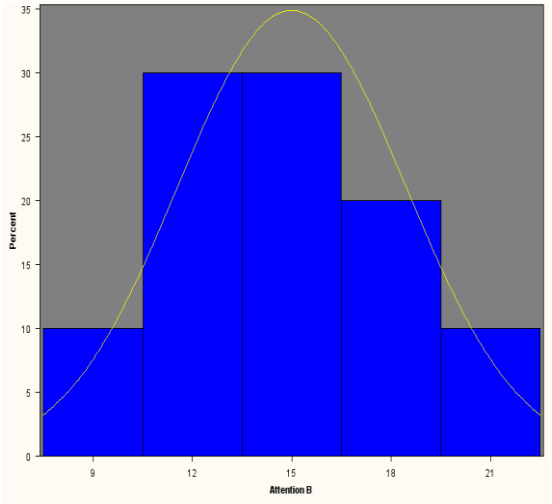
Comparison-CLQT-4 months-Visual Spatial



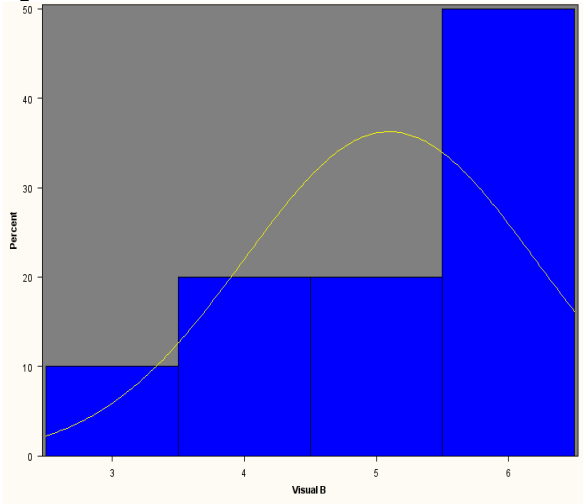
Comparison – IS-Baseline -4 months-Memory



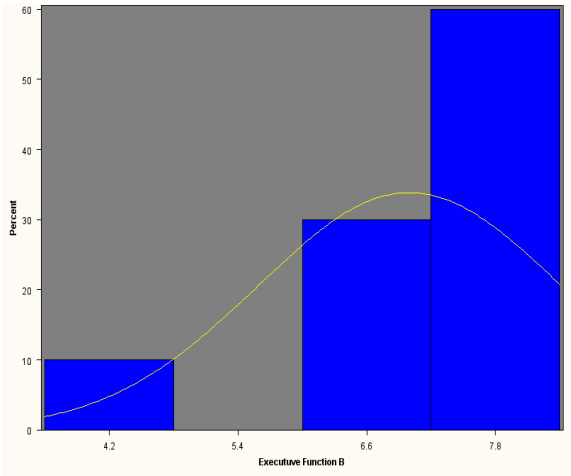
Comparison-IS-Baseline- 4 months-Attention



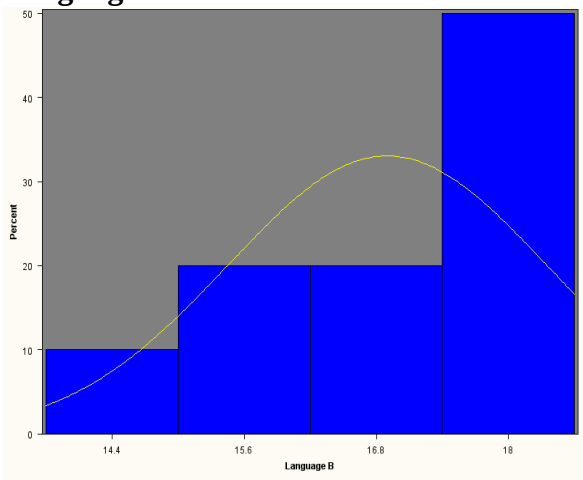
Comparison-IS-Baseline-4 months-Visual Spatial



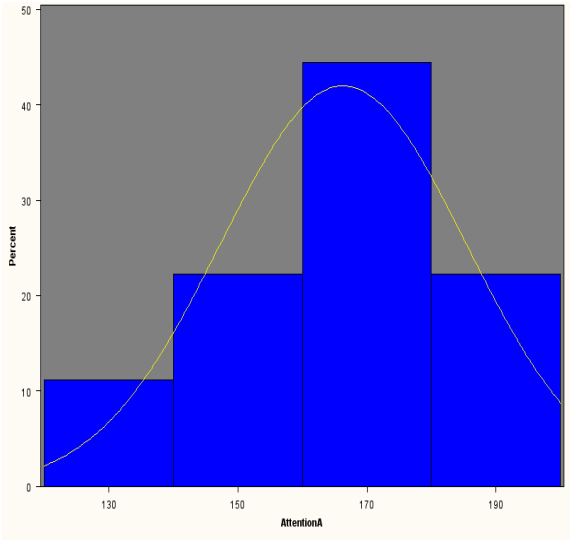
Comparison- IS-Baseline-4 months-Executive Function



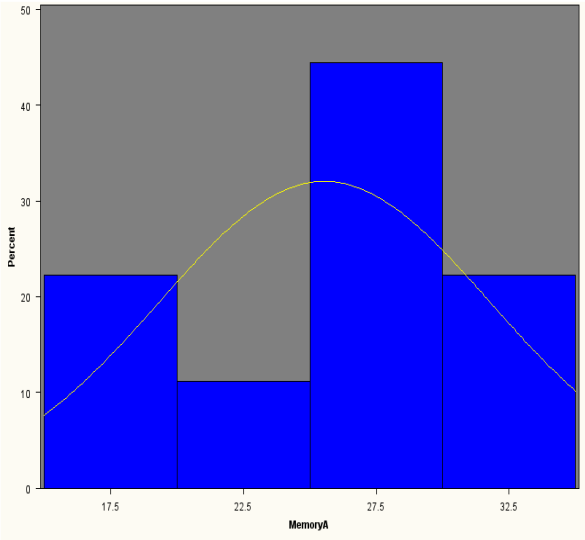
Comparison-IS-Baseline-4 months-Language



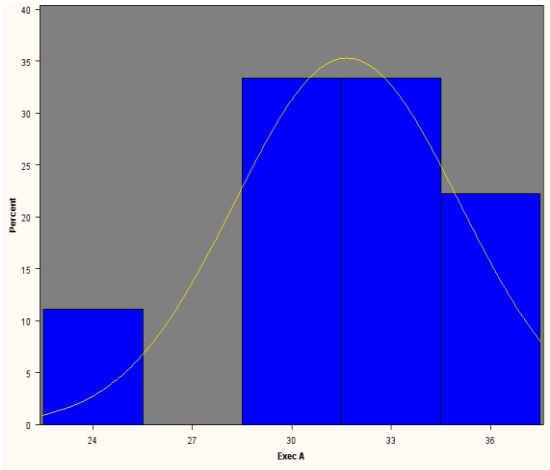
Comparison – CLQT – 8 months-Attention



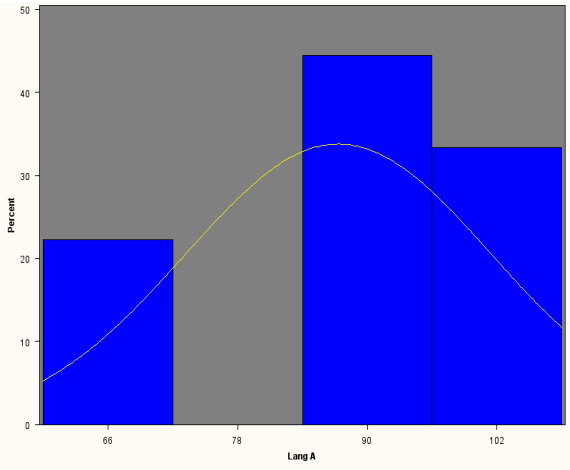
Comparison-CLQT-8months-Memory



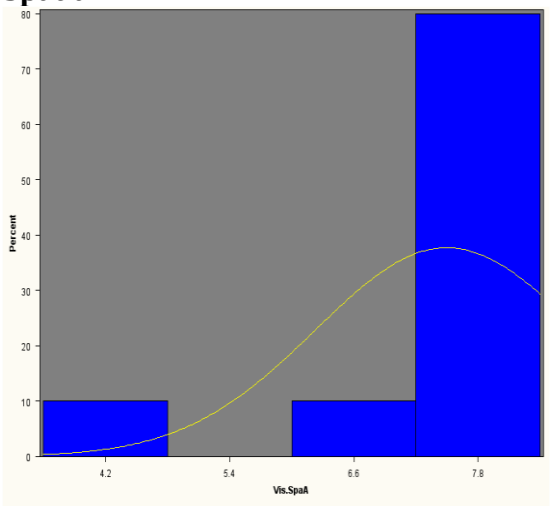
Comparison-CLQT- 8months-Executive Function



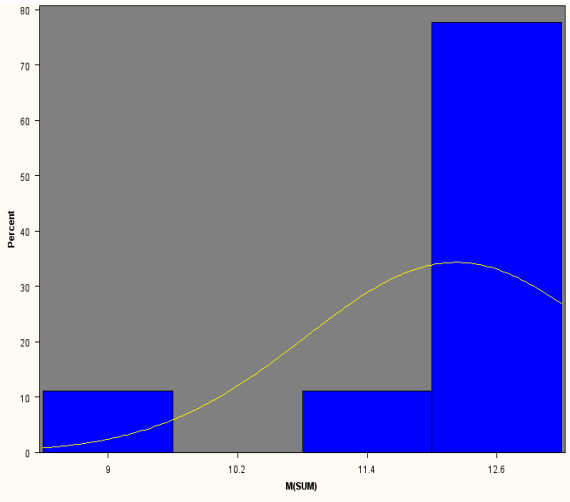
Comparison- CLQT- 8months-Language



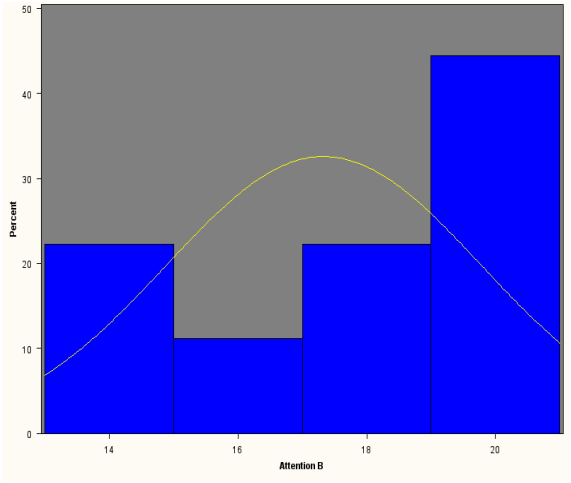
Comparison-CLQT-8 months-Visual Spatial



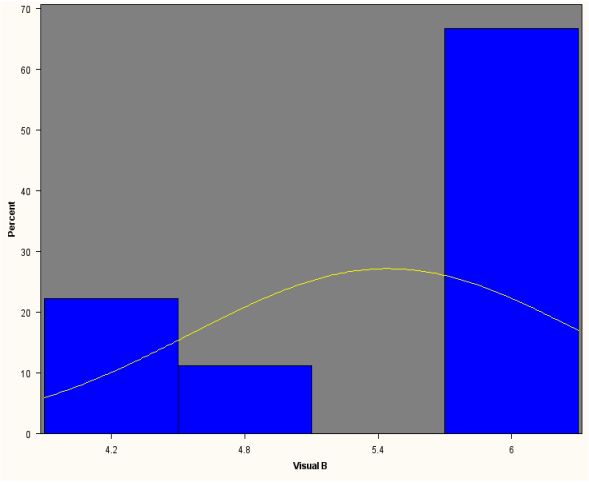
Comparison – IS - 8 months-Memory



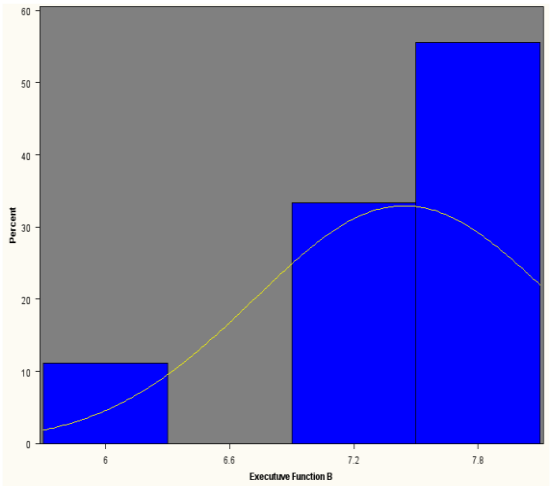
Comparison- IS-8 months-Attention



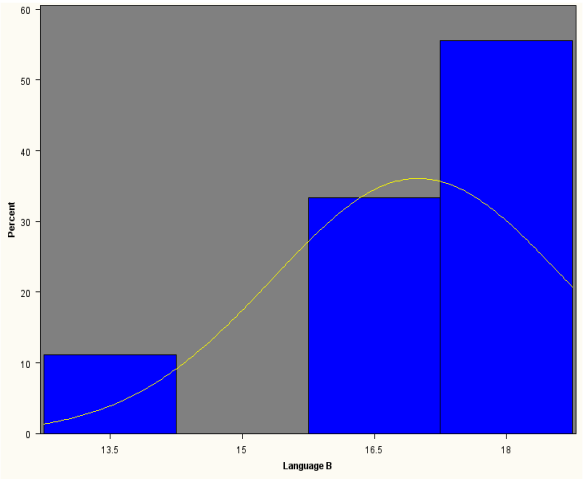
Comparison- IS-8 months-Visual Spatial



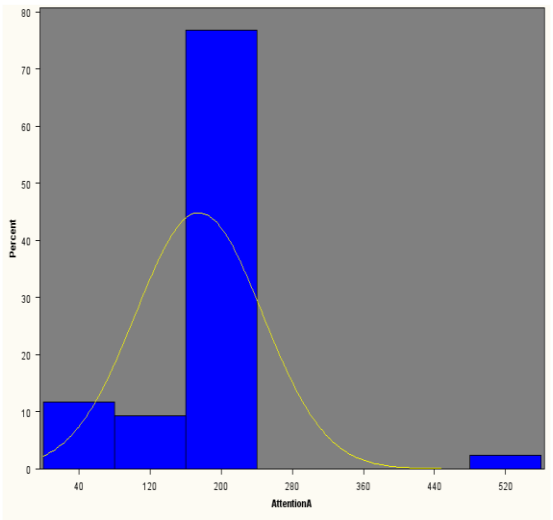
Comparison-IS -8 months-Executive Function



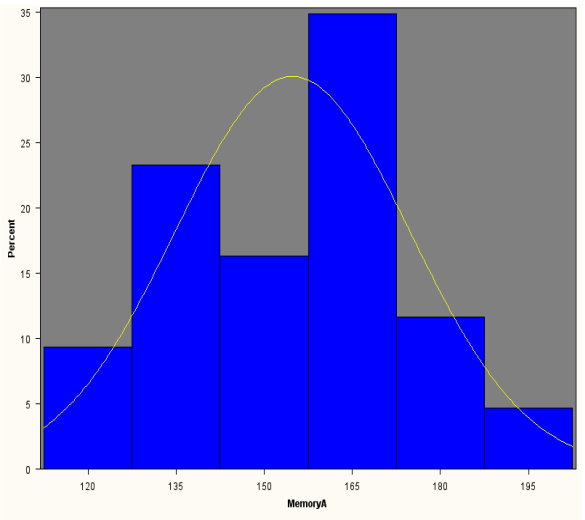
Comparison-IS-8months-Language



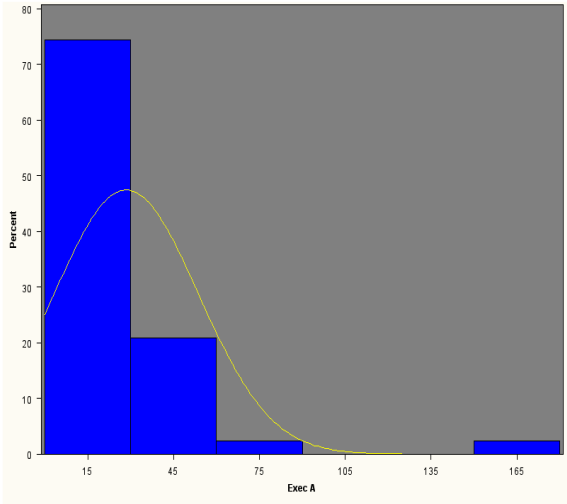
Cross Sectional-CLQT-4 months-Attention



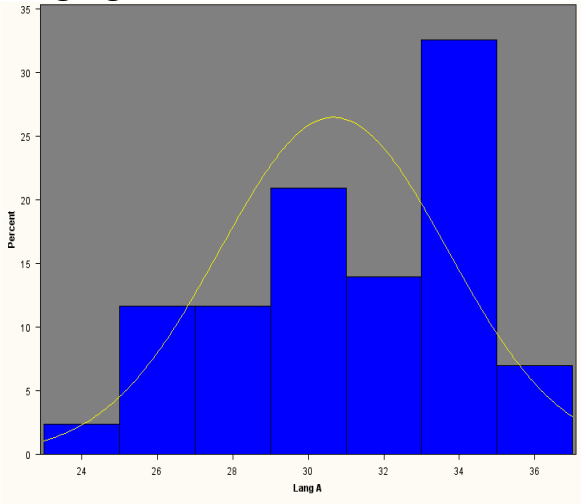
Cross Sectional-CLQT-4months-Memory



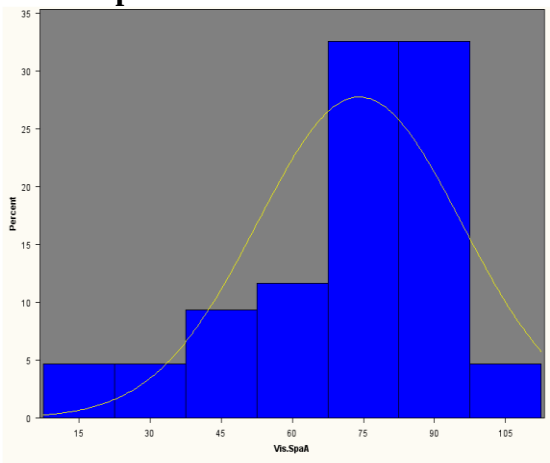
Cross Sectional –CLQT-4 months-Executive Function



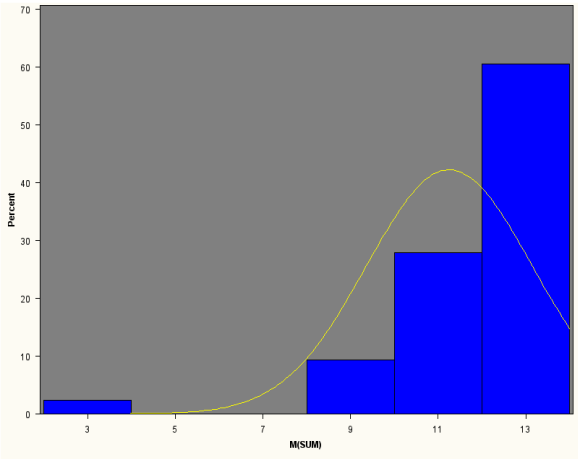
Cross Sectional-CLQT-4 months-Language



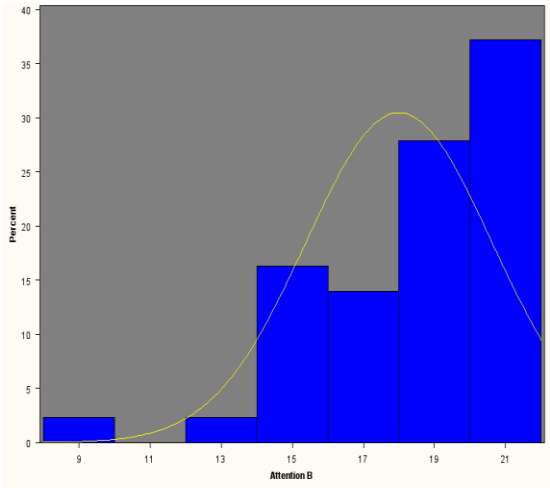
Cross Sectional-CLQT-4 months-Visual Spatial



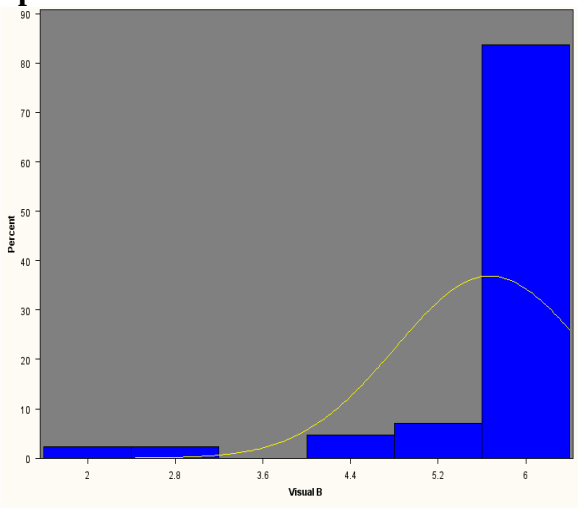
Cross Sectional-IS- 4 months-Memory



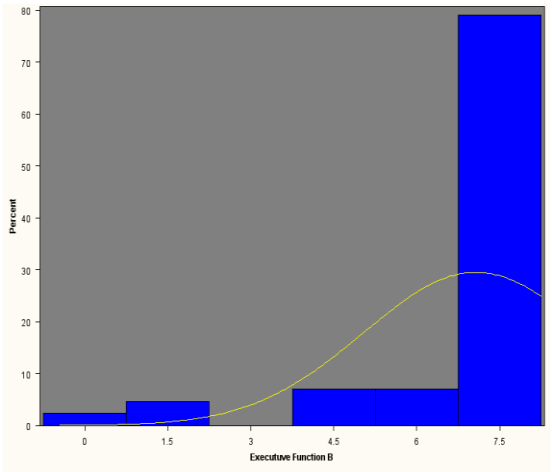
Cross Sectional-IS-4 months-Attention



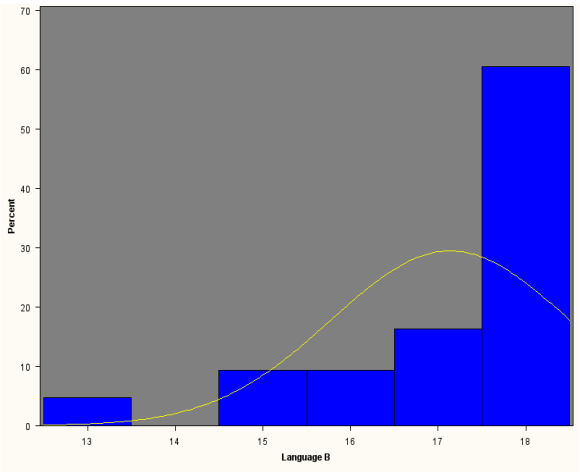
Cross Sectional-IS-4 months-Visual Spatial



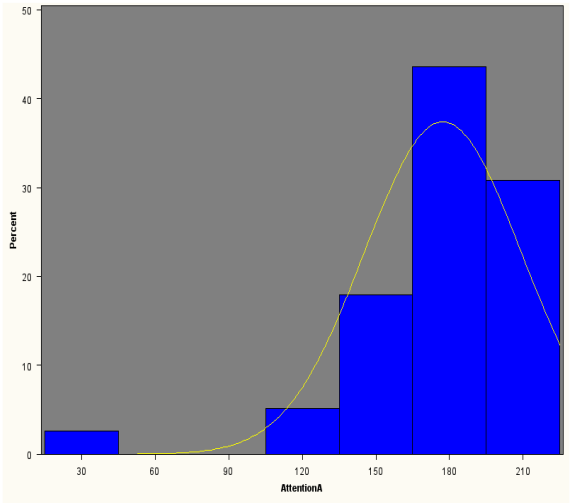
Cross Sectional-IS-4 months-Executive Function



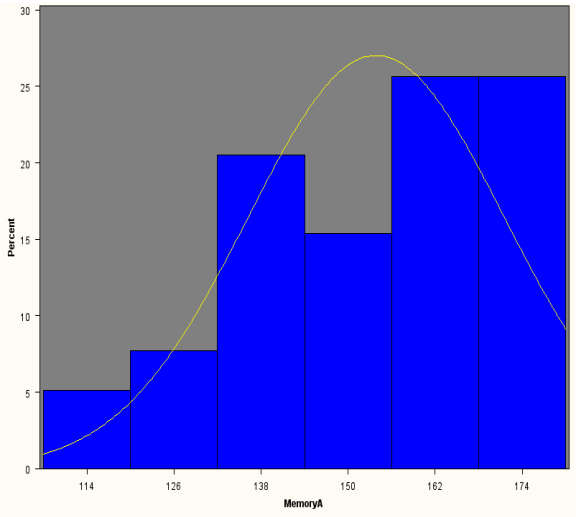
Cross Sectional-IS-4 months-Language



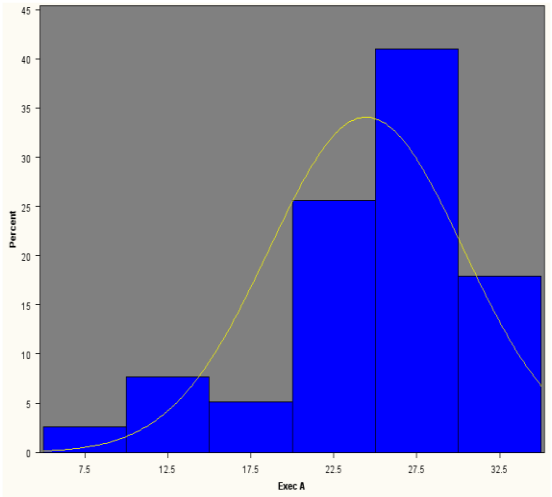
Cross sectional – CLQT -8 months-Attention



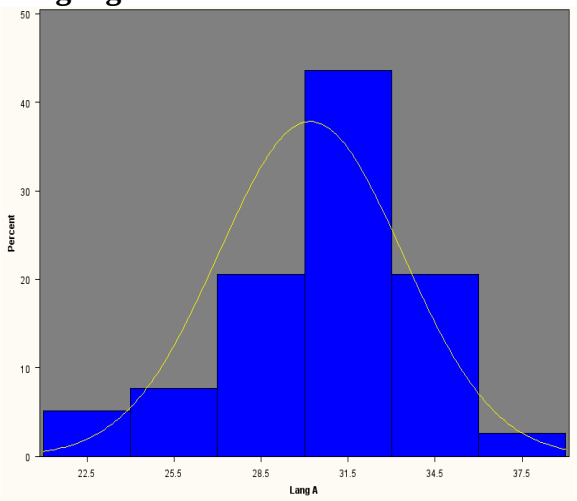
Cross Sectional-CLQT-8months-Memory



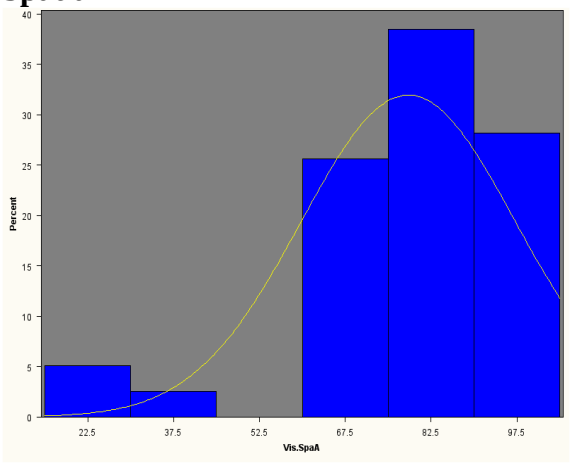
Cross Sectional-CLQT-8months-Executive Function



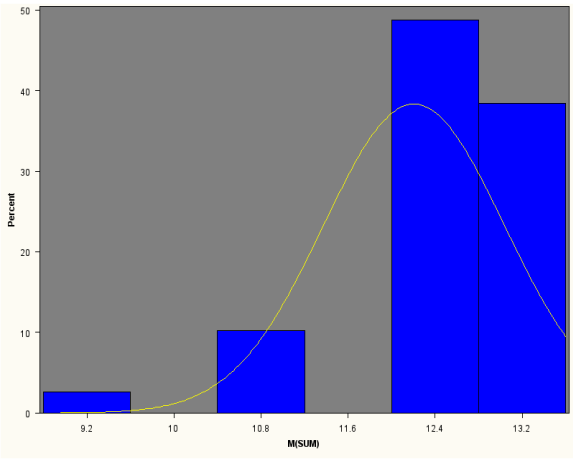
Cross Sectional-CLQT-8 months-Language



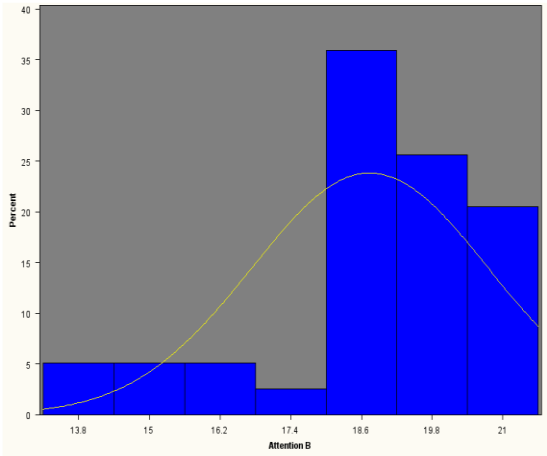
Cross Sectional-CLQT-8months-Visual Spatial



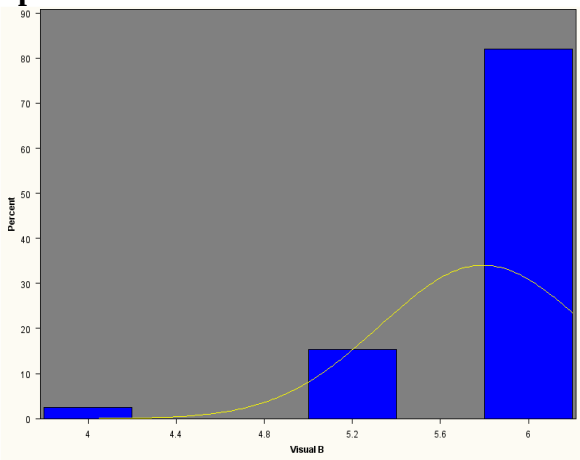
Cross sectional – IS- 8 months-Memory



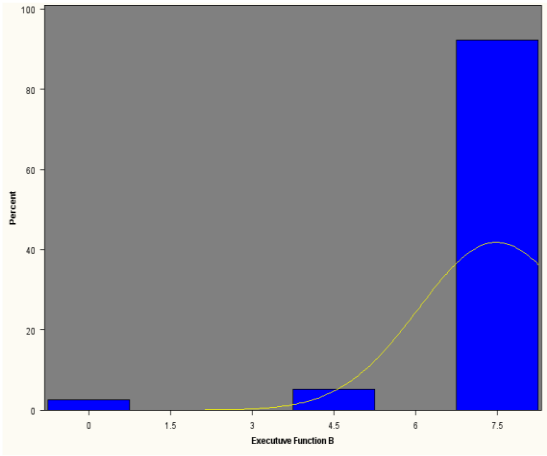
Cross Sectional-IS-8months-Attention



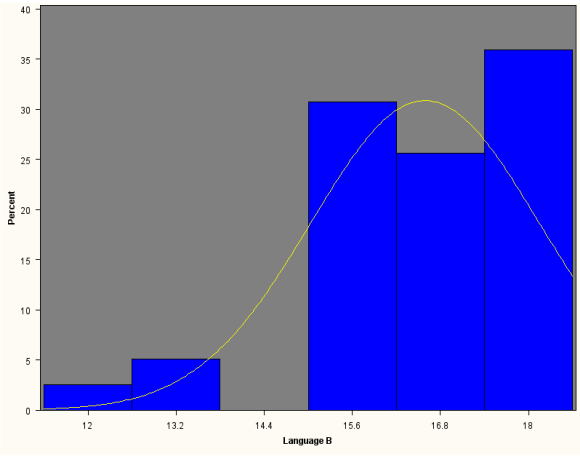
Cross Sectional-IS-8 months-Visual Spatial



Cross Sectional-IS-8 months-Executive Function



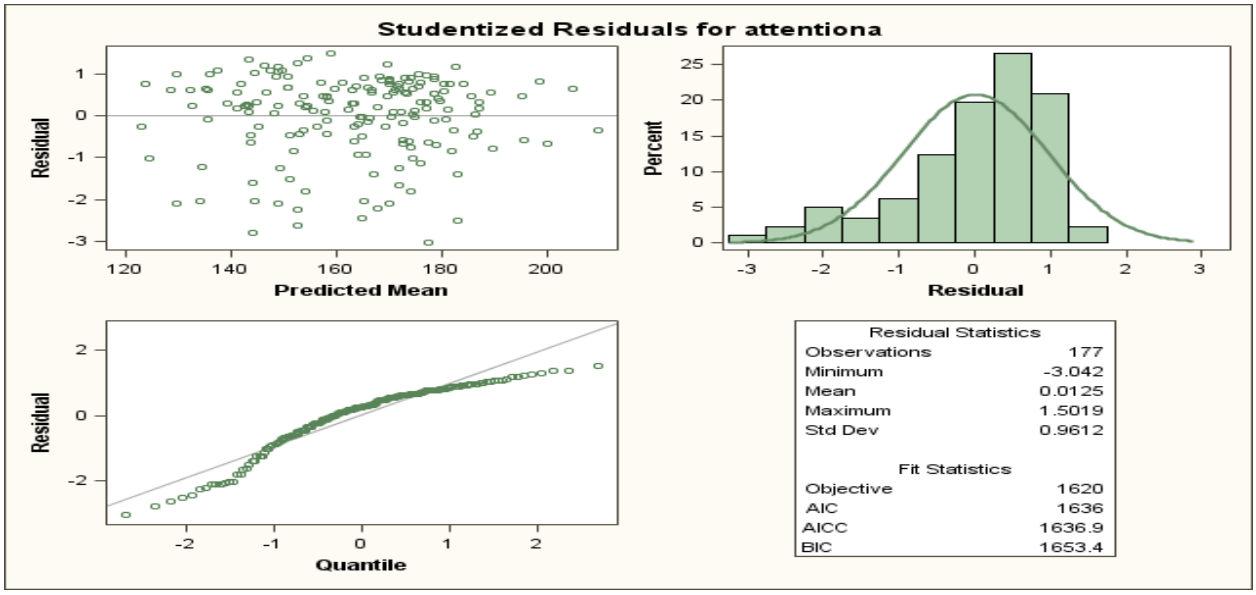
Cross Sectional-IS-8 months-Language



Appendix IX - Ancova Studentized Residuals

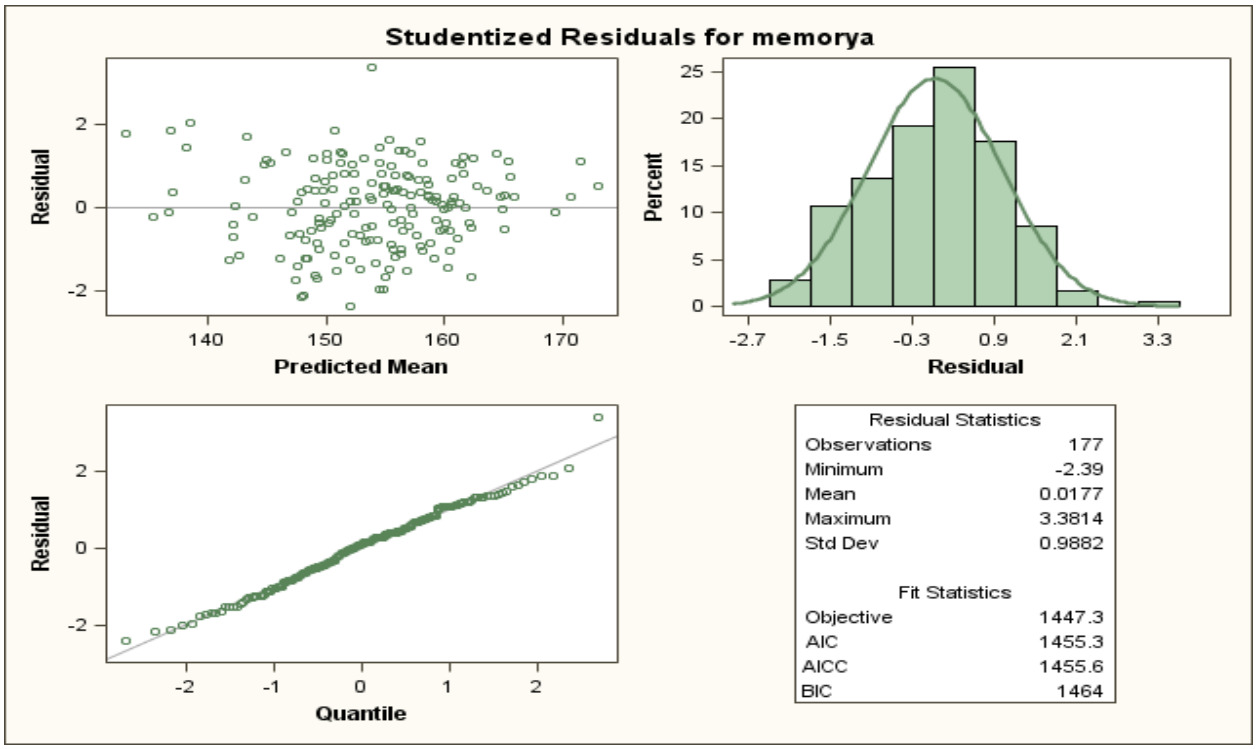
CLQT - Attention

Huynh-Feldt



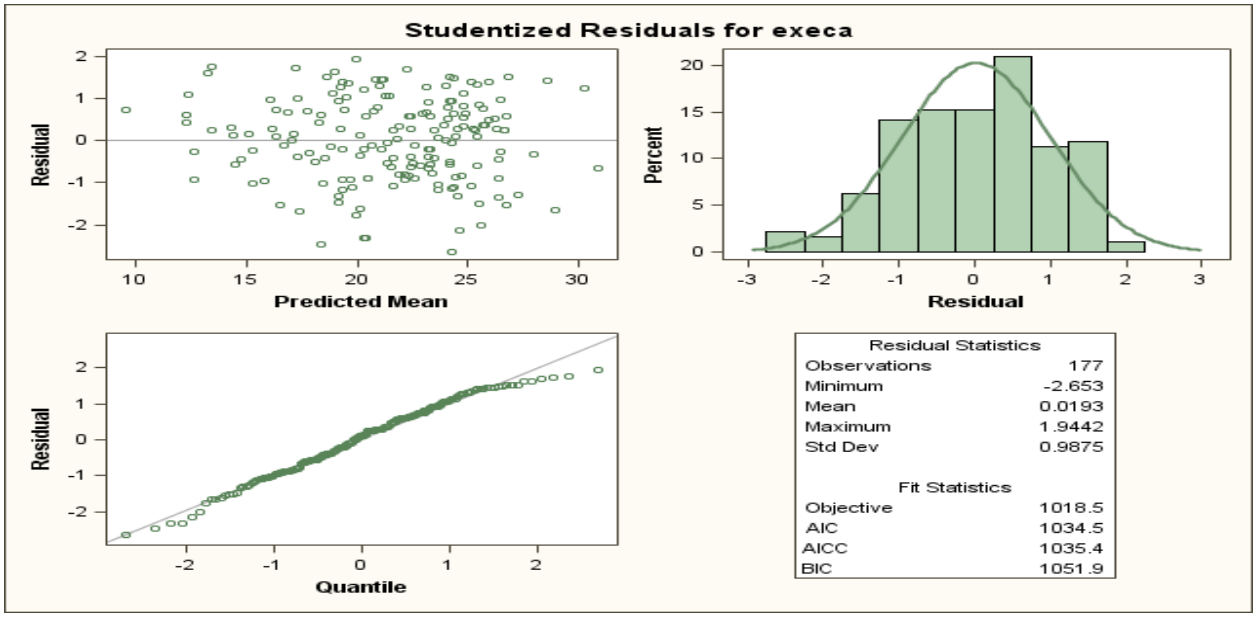
CLQT-Memory

Auto regressive
(1)



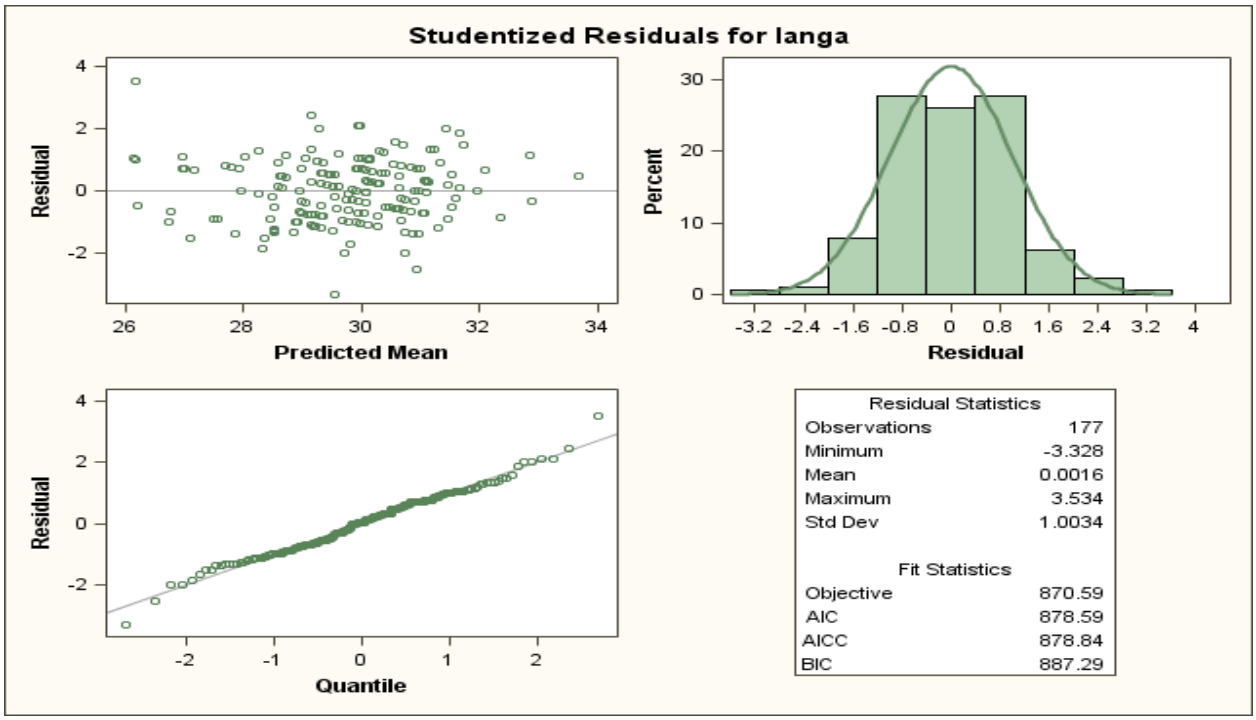
CLQT –Executive Functions

Huynh-Feldt



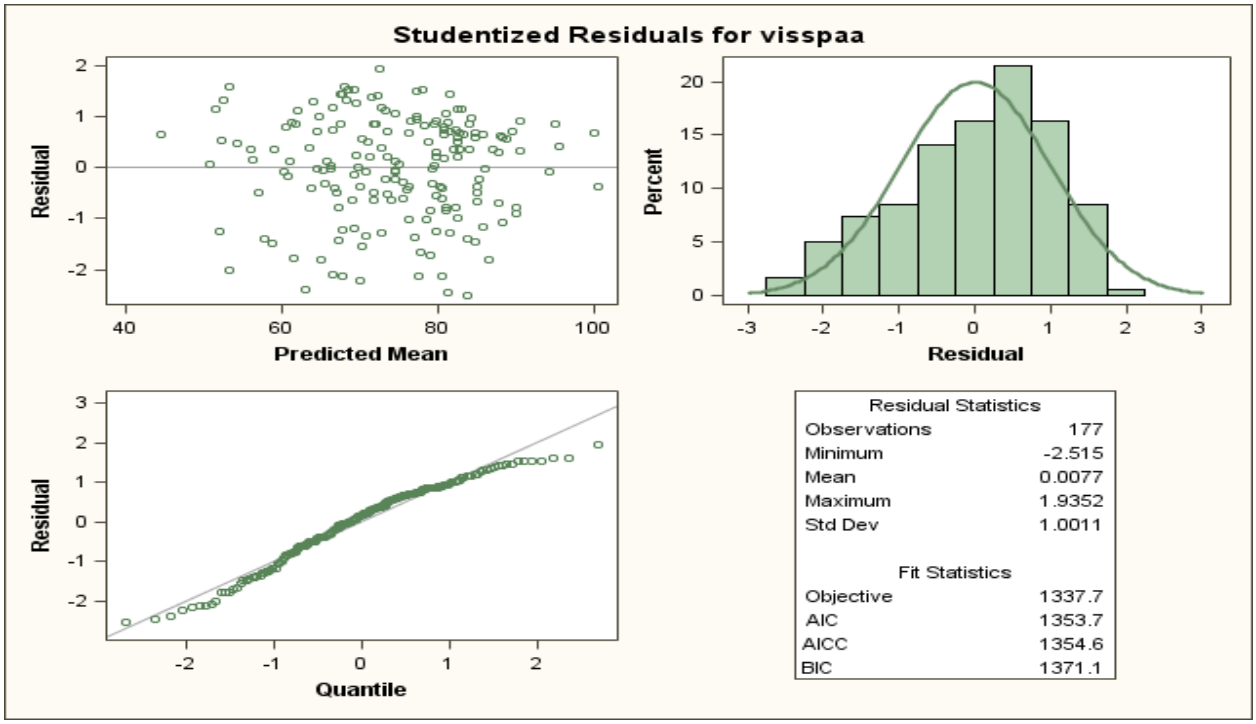
CLQT - Language

Autoregressive 1



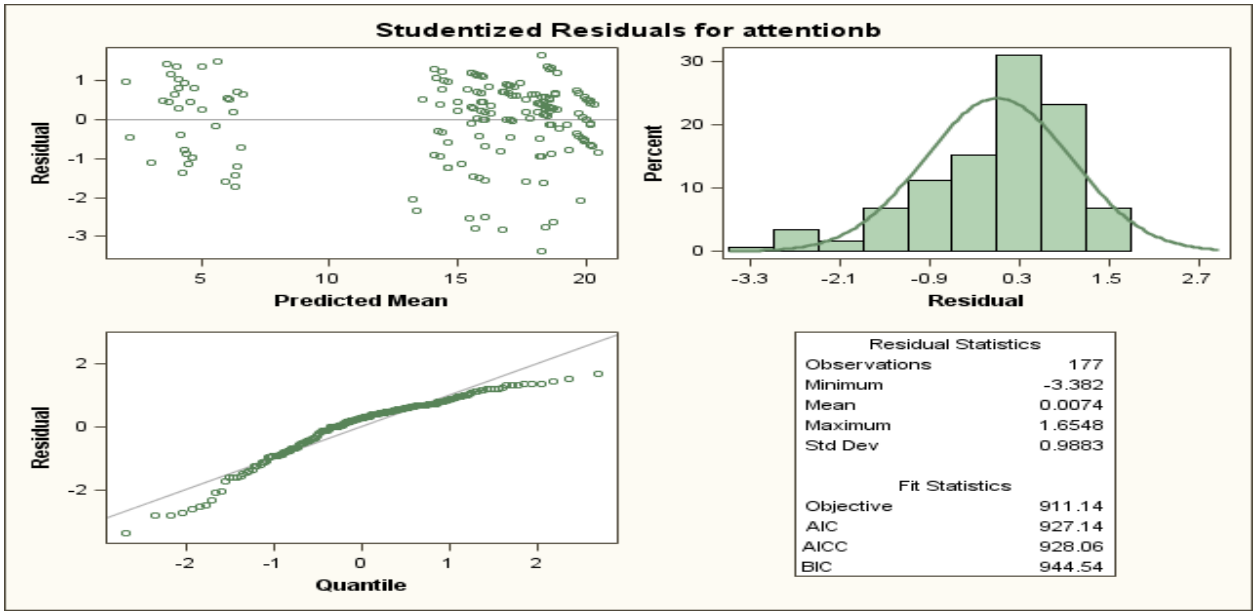
CLQT – Visual Spatial

Huynh-Feldt



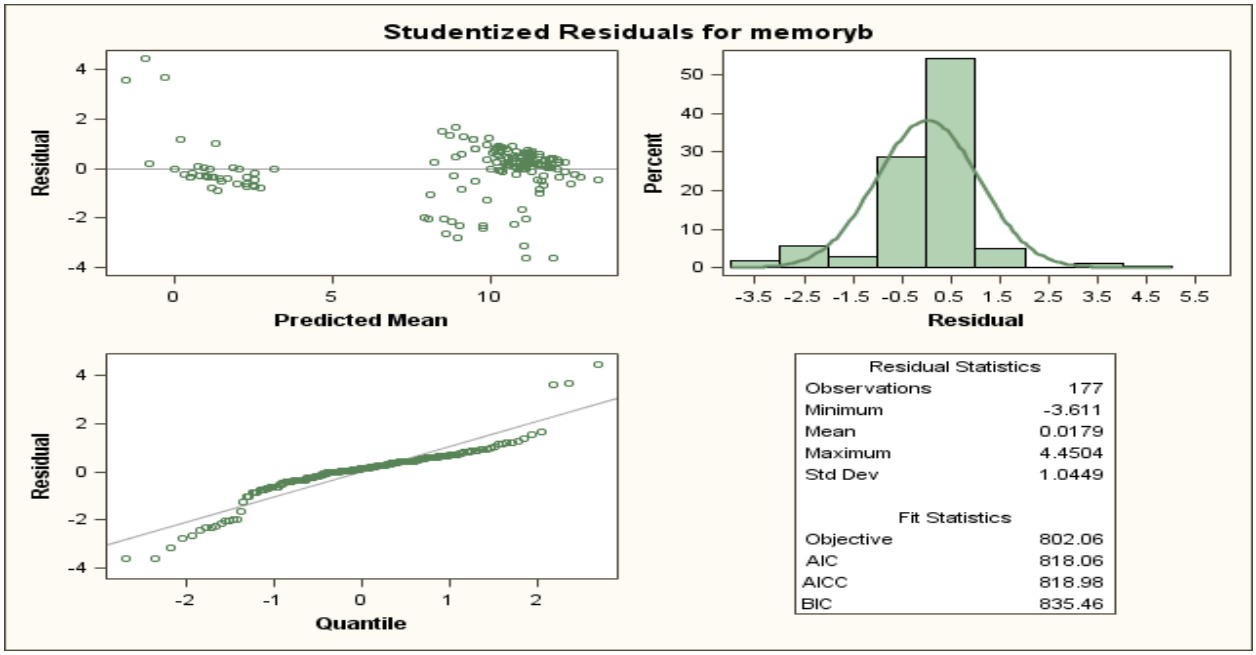
Interview schedule – Attention

Huynh-Feldt



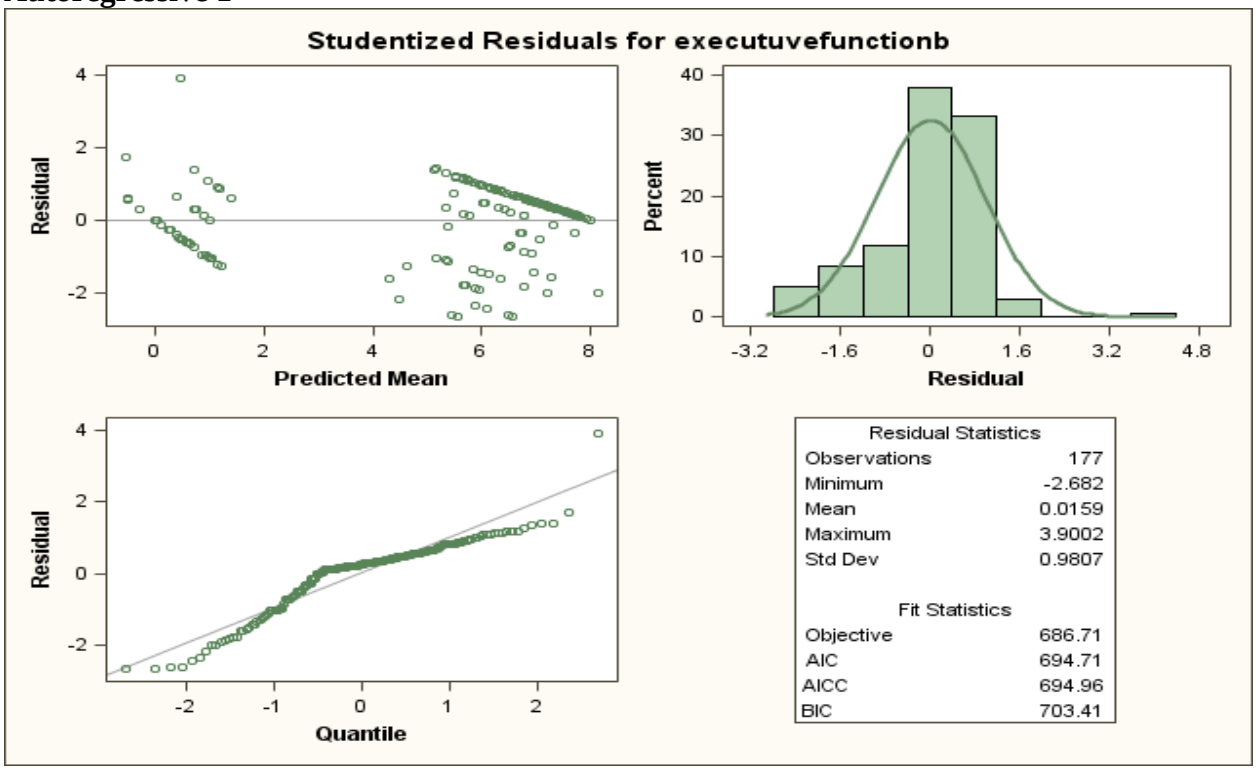
Interview Schedule – Memory

Huynh-Feldt



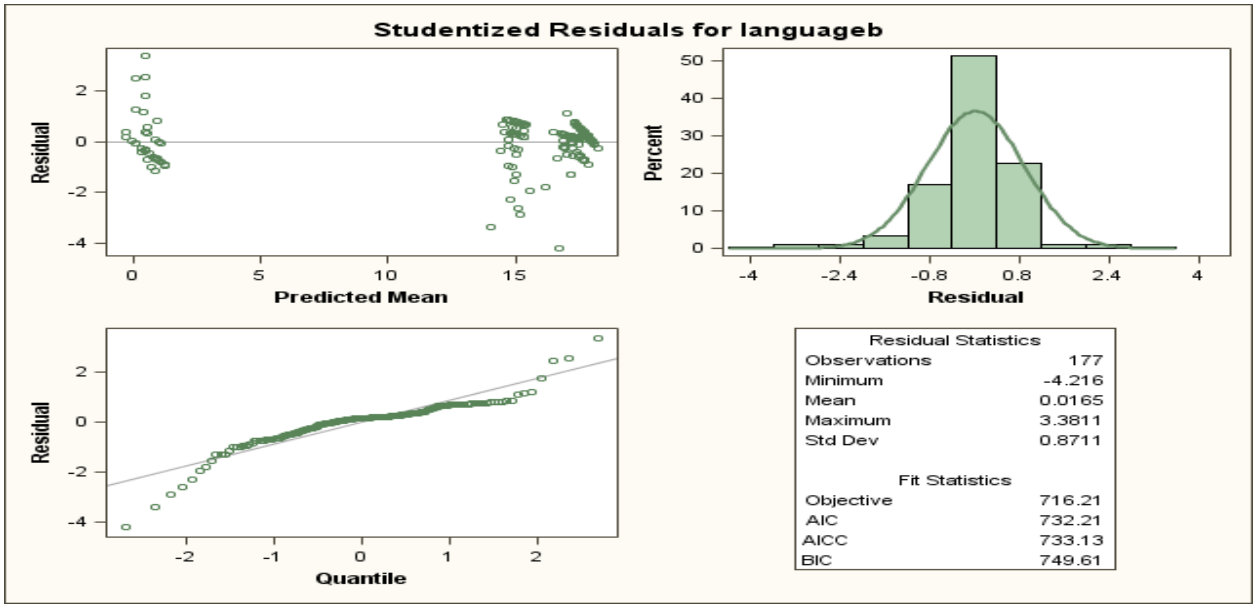
Interview Schedule – Executive Function

Autoregressive 1



Interview Schedule - Language

Huynh-Feldt



Interview Schedule – Visual Spatial

Huynh-Feldt