2008

Neuropsychological performance and dementia symptoms in a HIV positive population

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NEUROPSYCHOLOGICAL PERFORMANCE AND DEMENTIA SYMPTOMS IN A HIV
POSITIVE POPULATION

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

in

The Department of Psychology

by
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May 2008

Dedication

I wish to dedicate this document and my triumph through this period of my life to my parents John and Starley Kendra for all of their support during this process. Because of your love and encouragement I was able to endure the most difficult times. To mom, thank you for listening to the best and the worst, and always knowing how to help me see the good in myself and others. To dad, thank you for the unwavering reminders that I will be able to endure and succeed, and providing me with an example that inspired me to pursue my dreams.

For my brother Mark, for loving me for being myself. Throughout the years we've leaned on each other through the tough times and laughed with each other through the rest. Thank you for always being on my side so that I never feel totally alone. You are an incredible brother and friend.

To Jason, for dealing with me through the darker days and hanging in there even when I'm not sure I can. Thank you for your unconditional love and support and for believing in me when I struggled to believe in myself. I look forward to all of the wonderful times ahead, and have faith that we can rise to meet the challenges that present in the future and succeed together.

Finally, I would like to thank my dear friends Missy, Cindy and Laura for many years of sharing laughter and tears, and knowing you are always there for me. To Greg, Matt, and Isaac thanks for always bringing a smile to my face. I would like to extend my gratitude to Carla, Meredith, Amy, Scott, Adrianne, Kara, Kim S., Kim Z., Ryan, and Rinita for your kindness and friendship. I would also like to thank Theresa, Andy, Mindy, John and Nicole for pulling for me and for taking me in during my time of need. To Armin, Lara, Tiff, Kaci, Janice, Amit, Jill, Vickie, Rob, Simon, Bethany, and Denise, thank you for helping me let go of the past and enjoy the moment, and for showing me such genuine support.

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Abstract

Acquired immune deficiency syndrome (AIDS) is an infectious disease caused by human immunodeficiency virus (HIV), which affects millions of individuals worldwide. This syndrome is associated with many medical complications. Fortunately, patients with HIV and AIDS have longer life expectancy than in past decades with HIV and AIDS; however, the risk of cognitive impairment is greater in this population. Identification of dementia due to HIV/AIDS by health care professionals is hampered by the unclear relationship between cognitive functioning and HIV-related health status in the HIV/AIDS research literature. For the current study, individuals with HIV/AIDS who are symptomatic with infection but do not have an AIDS indicator condition (placing them in health classification group B) were categorized into one of two groups (G1 and G2) based on their t-cell count. This evaluation is important because subjects will likely have detectable neuropsychological impairments but will not be significantly impaired across all domains, allowing for more revealing comparisons. A brief neuropsychological battery was administered to all participants. Patients with more severe HIV-related health problems (as assessed by t-cell count) were expected to show greater cognitive-related impairments, and differences in neuropsychological classification ranges were expected across areas (e.g. motor, learning, etc.) depending on their current HIV-related status. Descriptive statistics were obtained for demographic variables, t-cell count, HIV symptoms, and health classification. Group means were compared to assess potential differences between the groups determined by t-cell count within the symptomatic without AIDS indicator health classification group. Follow-up analyses via regression were conducted to explore the relationships between variables. Findings indicate little differences between groups, but some groups differences were found while examining classification ranges.

Neuropsychological Performance and Dementia Symptoms in a HIV Positive Population

Acquired immune deficiency syndrome (AIDS) is an infectious disease, which compromises the immune system, and is caused by human immunodeficiency virus (HIV). While the disease first received medical attention in 1979, there is evidence that AIDS existed in the United States dating to 1970, and in Africa as far back as 1959 (Field, 1993). Often referred to as HIV-related dementia, HIV-1 associated dementia (HAD), AIDS-related dementia, or AIDS-D, the AIDS dementia complex (ADC) is considered to be one of the fastest growing dementia subtypes and the most common subtype in non-elderly individuals (Katona, 1989). ADC has been identified as the most common neurological complication associated with HIV infection, and it has been reported that most patients with ADC will experience cognitive decline at some point during the course of their illness (Navia, Jordan, & Price, 1986).

Estimates of the prevalence of HIV in the United States ranged from 1,039,000 to 1,185,000 (Glynn & Rhodes, 2005), and approximately 5 to 30% of these individuals have a diagnosis of HIV-related dementia (Ayers, Abrams, Newell, & Friedrich, 1987; Flaskerud, 1987; Honn & Bornstein, 2002). The percentage of AIDS dementia cases is likely underestimated within the AIDS population due to difficulties in identification and diagnosis (Tross, 1990).

The literature is unclear on the exact clinical presentation throughout the progression of cognitive decline to diagnosis of ADC among HIV positive (HIV+) persons. Becker, Lopez, Dew and Aizenstein (2004) found that, at baseline, a random sample of HIV+ patients were three times more likely to show cognitive impairment than non-HIV+ controls on measures of neuropsychological functioning. Further, cognitive impairments are hypothesized to occur more frequently during the later stages of HIV/AIDS (Davis et al., 2002) when approximately 20% of patients develop HIV-related dementia (Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999; De

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Ronchi et al., 2002). However, there are reports suggesting that up to 40% of patients experience cognitive decline even prior to being given a diagnosis of AIDS (Navia, Cho, Petito, & Price, 1986).

Although the trajectory of ADC remains unclear, there are data suggesting that among older adults, ADC is frequently the presenting AIDS illness (Becker, Lopez, Dew, & Aizenstein, 2004; Janssen, Okey, Selik, & Stehr-Green, 1992). As patients live longer with HIV, detection of ADC becomes even more important so as not to be confounded by age-related declines and symptoms associated with medical complications. Understanding the etiology of the cognitive impairment has prognostic and etiological implications, and may influence treatment planning.

Diagnosis of HIV Dementia

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychological Association, 2000) defines Dementia Due to HIV Disease as a disorder with a direct relationship with the presence and course of HIV. The dementia disorders require (1) memory impairment and (2) one or more of the following cognitive impairments: aphasia, apraxia, agnosia, or disturbance in executive functioning. Dementias typically cause significant occupational and social impairment, and are often characterized by gradual onset with declines occurring at a continuous rate. According to the DSM-IV-TR (APA, 2000), other medical conditions and Axis I disorders need to be ruled out before diagnosing a specific dementia. Specifiers include "without behavioral disturbance" and "with behavioral disturbance" which address symptoms such as wandering and agitation. The DSM-IV-TR indicates that symptoms of dementia due to HIV disease include forgetfulness, slowness, poor concentration, and impaired problem solving. Patients with HIV dementia disorder often present with apathy and social withdrawal.

Theoretical Models, Etiology, and Neuropathology

The brain reserve capacity (Satz, 1993) has been suggested to explain individual differences in susceptibility to ADC. This theory proposes that individuals with greater cognitive reserves (i.e. higher premorbid IQ, greater level of education, younger age) are less likely to develop ADC because their brain functions at a greater premorbid capacity. Thus, it would take more substantial cognitive declines for these individuals to present with dementia compared with older, less educated, lower IQ individuals (Satz, 1993).

Additionally, ADC has been described in a manner similar to other models of subcortical dementias (Arendt & von Giesen, 2002; Honn & Bornstein, 2002; Katona, 1989). Subcortical dementia suggests that the dementia involves nerve centers below the cerebral cortex in the brain. In subcortical dementias, patients typically present with the following impairments: psychomotor retardation, difficulty manipulating acquired knowledge, personality changes, and memory loss (Albert, Feldman, & Willis, 1974). As the major clinical features of ADC resemble these symptoms, it is often conceptualized using this framework.

Many persons with HIV/AIDS do not initially present with neurological abnormalities. Price and colleagues (1988) suggest that the immune system is able to suppress the neurological reaction until it becomes too weak, which is a sign of disease progression. Autopsies have revealed neuropathological evidence suggesting that ADC exists in more patients than present with observable clinical symptoms, suggesting the possibility that many patients with neurological lesions die before the dementia manifests clinically (Vago, Trabattoni, Lechi, Cristina, & Budka, 1990). In the Vago et al. (1990) study, the majority of patients were HIV asymptomatic and had neuropathological evidence of dementia. However, in all of the patients where myelin abnormalities were found, neurological impairments were demonstrated in their

clinical presentation. Thus, while it appears that current measures for assessing and diagnosing ADC lack sensitivity, individuals with organic damage eventually manifest the damage behaviorally or cognitively, and the onset of de-myelinization marks the period where clear neurological symptoms are observed.

The "Trojan Horse Hypothesis" (Haase, 1986; Peluso, Haase, Stowring, Edwards, & Ventura, 1985) suggests that the ADC may result from the HIV virus entering into cells that have the ability to cross the blood-brain barrier. Once the cell enters the brain, neuronal loss may occur through neurotoxic proteins or microglial infection causing ADC in the brain which, leads to clinical manifestation stemming from neuronal damage (Ghafouri, Amini, Khalili, & Sawaya, 2006).

Premorbid Variables and Biological Markers

Older age, lower levels of education, lower premorbid IQ, and lower occupational attainment have been identified as risk factors for the onset of AIDS related dementia (Basso & Bornstein, 2000; Becker, Lopez, Dew, & Aizenstein, 2004; De Ronchi et al., 2002; Schmand, Smit, Geerlings, & Lindeboom, 1997). Additionally, additive risk factors are also associated with number of AIDS defining illness, dementia, and death (Farinpour et al., 2003). For example, being older, having lower IQ and less education makes one more likely to meet criteria than having lower IQ alone.

One biological marker that is often used to identify severity and prognosis in individuals with HIV is the cluster of differentiation 4 (also known as CD4 count and t-cell count). Surprisingly, there is little evidence to suggest that there is a significant association between CD4 count and the prediction of neuropsychological impairment (Honn & Bornstein, 2002). However, there is evidence that CD4 counts decline as neuropsychological impairment worsens

(Bornstein et al., 1991; De Ronchi et al., 2002). This is interesting because CD4 count is often used as a marker for health status in patients with HIV/AIDS and is used in predicting and preventing related negative health outcomes, yet the value of CD4 count in ADC appears to be considered less predictive or informative.

Plasma viral load, another biological marker of HIV, is considered to be weak and unreliably correlated with dementia symptoms (McArthur, 2004). However, plasma viral load correlates positively with reaction time, although not overall psychomotor slowing (Cysique, Maruff, Darby, & Brew, 2006), with higher viral loads more frequently occurring in HIV dementia groups as compared to HIV-Minor Cognitive Motor Disorder (HIV-MCMD) groups (Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999). Lower CD4 and elevated plasma viral load are associated with impairments in executive functioning (Chang, Ernst, Witt, Ames, Gaiefsky, & Miller, 2002) as measured by performance on a Stroop task. These findings suggest that while plasma viral load may not be a significant marker of HIV-related dementia, declined health status may indicate impairments in neuropsychological functioning.

Cerebrospinal fluid (CSF) viral load, while a more invasive measure of assessment, may also be used as a biological marker of HIV severity. Gonzalez and colleagues (2003) found that traditional neuropsychological batteries (e.g. Halstead-Reitan and the Wechsler series), which have historically been deemed the "gold standard" measurement of cognitive decline, to have a slightly better association with biological markers (i.e. CD4 count and CSF viral load) of HIV than computerized reaction time tests that assess processing speed and complex motor skills. In addition, Gonzalez and colleagues found that measures examining these two domains from the traditional neuropsychological battery consistently demonstrated greater associations with detectable CSF viral load and CD4 count, which suggests that motor and processing speed may

be more sensitive to HIV-associated cognitive impairments than other areas of cognitive functioning.

Stage of disease as determined by medical doctors is also used, albeit less often, as a framework for the analysis of cognitive impairment. Becker, Lopez, Dew and Aizenstein (2004) found that disease stage, at baseline, was a significant predictor of subsequent cognitive impairment. This suggests that factors that impact HIV-related health, may contribute to the course and severity of cognitive related impairment. That is, it may be possible that by using disease stage, severity of cognitive impairment could be predicted. The current study sought to explore the extent that stage of disease has on degree of neuropsychological impairment.

Disease Course

While data suggests a progression of cognitive decline in persons with ADC, the exact course of impairment is less clear. Catalan and Burgess (1996) suggest that ADC is associated with poor prognosis. Once developed, ADC can become much more severe in a matter of months. There is evidence that significant cognitive decline generally does not occur in asymptomatic HIV+ individuals (Catalan & Burgess, 1996; Grant, Marcotte, Heaton, & HNRC group, 1999). However, these asymptomatic individuals may perform more poorly on neuropsychological measures than their non-HIV+ counterparts. This may indicate that asymptomatic patients are in the early onset stages of dementia, similar to their "asymptomatic" HIV medical status.

Subcortical dementias, such as dementia associated with multiple sclerosis, show a positive correlation between disease progression and severity of cognitive decline (Calabrese, 2006; Grant, Marcotte, Heaton, and the HNRC group, 1999). This course is less well-defined in the ADC literature. Different attempts have been made to categorize the progression of ADC.

One such attempt is through the coining of the term HIV-Minor Cognitive Motor Disorder (HIV-MCMD) (Navia, Cho, Petito, & Price, 1986). Motor impairment has been found to be an early marker of ADC (Chang, Ernst, Witt, Ames, Gaiefsky, & Miller, 2002; Selnes et al., 1991). This addresses the notion that there are markers (e.g. motor impairment) that indicate the early symptoms or presence of cognitive decline (Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999).

Individuals with HIV and AIDS may experience physiological symptoms before they begin to experience cognitive decline. These symptoms may include night sweats, diarrhea, fatigue, weight loss, fever, hacking cough, pain and aches, and enlarged lymph nodes (Tross, 1990). In some cases, cognitive decline presents as the first symptom of AIDS, before other physiological symptoms. Conversely, Janssen, Okey, Selik, and Stehr-Green (1992) reported that dementia occurred almost exclusively in patients with advanced AIDS who are already experiencing other physical symptoms.

In the early stages of ADC, traditional mental status testing and even neuroimaging may not show significant impairments (i.e. in patients with HIV-MCMD). However, further along the course of HIV-related dementia, mental status assessments of attention, concentration, and memory do show impairments. In addition, cerebral atrophy can be seen using MRIs as patients move into the more severe stages of ADC (Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999). Tross (1990) reported that initially ADC presents predominantly with cognitive symptoms, especially processing speed and memory deficits. In addition, she reported that 33% of patients present with primarily two behavioral symptoms: increased apathy and withdrawal.

The introduction of highly active antiretroviral therapy (HAART), while inarguably of great health benefit to the patient, confounds research with ADC because biological markers tend to show improvements relatively quickly after the initiation of treatment. However, cognitive

deficits tend to improve much more slowly, taking up to a year for treatment effects to become evident (Sacktor et al., 1998; Stankoff et al., 2001). Empirical support exists for the notion that HAART may prevent or reverse cognitive declines, although further research is needed to confirm these results (De Ronchi et al., 2002; Gonzalez et al., 2003; Stankoff et al., 2001).

The course of cognitive decline in the ADC is varied and understudied. Navia et al. (1986) reported that within two months of ADC detection, half of their subjects presented with severe neurological impairment. Tross and Hirsch (1988) reported that in the later stages, HIV-related dementia may resemble the advanced stages of "a full-blown, incapacitating, geriatric-like dementia" (page 932). It is unclear how patients who are in the "middle stages" of the disease experience cognitive dysfunction. Prior research has addressed clinical presentation in patients in the early stages of HIV+ health status (Maruff et al., 1994; Sidtis & Price, 1990). Likewise, there is literature pertaining to the impairments found in the later or "end stages" (Tross & Hirsch, 1998). However, no research, to date, appears to address clinical neuropsychological performance specifically in patients who are symptomatic with HIV infection but without AIDS indicator condition(s).

Neuropsychological and Psychological Functioning Associated with HIV-Related Dementia

In the early stages of ADC, neuropsychological tests may be used to identify subtle cognitive deficits (Field, 1993). Individuals with ADC present with cognitive, motor, and behavioral disturbances (Horwath, Kramer, Cournos, Empfield, & Gerwirtz, 1989). Early cognitive symptoms of ADC include: slowness, impaired attention and concentration, forgetfulness, and confusion (Buckingham & Van Gorp, 1988; Navia, Jordan, and Price, 1986). Deficits in processing speed, learning, language, executive functioning, and motor domains are also found in ADC patients (Carey et al., 2004; Grant, Marcotte, Heaton, & HNRC Group,

1999). In their study, Maruff and colleagues (1994) found that the early neuropsychological symptoms of ADC were restricted to specific areas of functioning including: executive functioning, memory, and complex attention. As in the other subcortical dementias, deficits in intelligence most often indicate a progression of the HIV-related dementia into the more severe stages (Buckingham & Van Gorp, 1988). Lower Shipley Institute of Living scores have been associated with shortened time to dementia (Farinpour, Miller, Satz, Selnes, Cohen, et al., 2003).

According to Everall (1995), HIV-related dementia usually presents without apraxia or agnosia, but with memory loss and difficulties in retrieval and manipulation of information. Thought processes are typically slowed and deficits in processing speed are commonly the earliest symptom to appear in subcortical dementias, which may contribute to subsequent deficits in memory and executive functioning (Calabrese, 2006). In the beginning stages of ADC, patients commonly demonstrate difficulties with fine motor speed and control. Early motor impairments include clumsiness, deterioration of fine motor skills, tremor, loss of balance, leg weakness, and deterioration in handwriting (Everall, 1995; Navia, Jordan, & Price, 1986).

Emotional disturbances such as depression and changes in personality are also common initial presenting symptoms (Arendt & von Giesen, 2002; Buckingham & Van Gorp, 1988). Navia (1990) reported that friends, family, and colleagues will frequently report observing that the patient has lost spontaneity and has withdrawn and become disinterested in group activities before other symptoms of ADC became evident. The overall clinical presentation may be described as a transformation from an individual who was productive and energetic, into a person who is dull, apathetic, and subdued. Everall (1995) stated that behaviorally, apathy and social withdrawal can easily be mistaken for depression.

In later ADC, impaired performance is also found in verbal fluency, verbal and visual memory, and visual-spatial performance (Field, 1993; Navia, 1990). In addition, Navia also stated that research has consistently found that language functioning generally remains intact in patients with ADC, except in limited severe cases. However, speech may be slowed and volume may be lower than premorbid levels (Buckingham & Van Gorp, 1988). The visual-spatial deficits, according to Buckingham and Van Gorp are relatively severe throughout the course of ADC and create problems with navigation and figure copying. As the dementia worsens, so do the cognitive and physical declines, and symptoms can become as severe as incontinence and muteness (Everall, 1995). Thus, it appears that the current literature has addressed what the common initial presenting neuropsychological symptoms are as well as what impairments are evident in the later stages of ADC. However, it is unclear what the clinical presentation is of individuals who are in the "middle stages" of AIDS related dementia.

Assessment of HIV Impairment

Portegies and Rosenberg (1998) reported that a neuropsychological assessment is essential to the diagnosis of ADC. Neuropsychological tests may be used to assess for severity of problems, and re-evaluation may be useful in the determination of treatment effectiveness. According to these researchers, a comprehensive assessment of ADC should evaluate: complex sequencing, psychomotor abilities, fine and rapid motor movement, and verbal fluency. Sidtis and Price (1990) add that tests intended for use in the diagnosis of ADC should be timed as opposed to untimed, involve attention and concentration components, and emphasize precise and rapid motor skills.

According the material presented at the 4/10-11/89 NIMH Workshop entitled "Neuropsychological Assessment Approaches", neuropsychological batteries should directly

assess the areas that are most likely to be deficient. In particular, tests focusing on attention and processing speed should be present (Butters et al., 1990). Cysique, Maruff, Darby, and Brew (2006) attempted to replicate prior research findings using a computerized test battery and confirmed that basic areas necessary for evaluation of cognitive functioning in HIV+ populations include attention, psychomotor speed and motor function, learning, and memory.

While the existing literature includes several measures that are commonly used and widely accepted in the assessment of dementia due to HIV, there is not a specific battery or empirically validated "gold standard". Traditional batteries, such as certain measures from the Halstead-Reitan Battery, measures assessing memory, and the Wechsler Adult Intelligence Scales appear to be the most frequently used (Gonzalez et al., 2003). The aforementioned 1989 NIMH workshop continues to be the guiding force in determining which measures to use to assess HIV-related cognitive declines (Carey et al., 2004; Gonzalez et al., 2003).

Tests that have consistently been used in the assessment of ADC and show presence of and changes in neuropsychological functioning in persons with HIV include: Grooved Pegboard (Klove, 1963, Matthews and Klove, 1964) and Finger Tapping Test (FTT; Heaton, Grant, & Matthews, 1991) (fine motor skills), Trail Making A and B (TMT; Partington & Leiter, 1949) and Digit Symbol on the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) (processing speed and sequential problem solving), Information, Comprehension, and Similarities on the WAIS-III (Wechsler, 1997), Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983) (language) Controlled Oral Word Association Test (FAS: Benton and Hamsher, 1976; Benton, Hamsher, & Sivan., 1983) (verbal fluency and spontaneity), Block Design (WAIS-III; Wechsler, 1997) (visuospatial skills), the Rey Complex Figure Test (RCFT; Rey, 1941) (visual memory), Stroop Color Interference Test (Stroop, 1935) (executive

functioning), Center for Epidemiologic Studies- Depression Scale (CES-D; Radloff, 1977), Minnesota Multiphasic Personality Inventory-2, (MMPI-2: Butcher et al., 2001) (mood and personality), and the Wechsler Memory Scale-Third Edition (WMS-III: Wechsler, 1997) (visual and verbal memory) (Becker, Lopez, Dew, & Aizenstein, 2004; Chang, Ernst, Witt, Ames, Gaiefsky, & Miller, 2002; Everall, 1995; Greenwood, 1991; Gonzalez et al., 2003; Navia, 1990). However, while these are the tests most commonly used for assessment of ADC, there is no current literature to describe the evolving course of the disease or to explain the order in which these areas of functioning become impaired (Everall, 1995).

Due to the high rates of depression and anxiety among HIV+ individuals, scales that assess mood should be included as part of the neuropsychological battery (Butters et al., 1990). Depression and ADC share several symptoms and are often difficult to distinguish from one another. Shared symptoms include anhedonia (i.e., inability to experience pleasure), sleep disturbance, appetite disturbance and weight loss, lack of energy and lack of sexual desire. The clinician must therefore assess factors such as self-esteem, guilt, and suicidal ideation to make the differential diagnosis, as these symptoms are more characteristic of depression (Field, 1993).

In addition, high scores on measures of depression have been associated with shortened time to diagnosis of ADC (Farinpour, Miller, Satz, Selnes, Cohen, et al., 2003). However, many studies have failed to find a significant relationship between depressive symptoms and performance on memory tasks in HIV+ populations (Goggin et al., 1997). Goggin and colleagues (1997) further expand that these inconsistent findings may be due to the use of brief screenings and self-report measures used to assess for mood which may increase the appearance of a strong positive relationship. Goggin used a more comprehensive battery (extended Halstead-Reitan), which yielded no significant relationship between depression and

neuropsychological impairment. Honn and Bornstein (2002) proposed an indirect relationship between neuropsychological functioning and depression in HIV+ individuals. They suggested that impaired neuropsychological performance contributed to increased levels of illness-related dysfunction. This perception of greater disability may result in higher levels of depression. Assessing stage of disease may be useful for determining which patients are more likely to report depressive symptoms.

A mental status exam is also important in the assessment of ADC, as it may reveal psychomotor slowing, impaired word reversal, serial subtraction, blunted affect, and organic psychosis (Navia et al., 1986). Portegies and Rosenberg (1998) stated that the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) score may be normal, but responses are delayed in persons with ADC. Thus, as is the case with other cognitive disorders, this measure is appropriately used only as a screening tool, and not as the primary diagnostic test. However, the MMSE and other screeners such as the Mattis Dementia Rating Scale (DRS; Mattis, 1973) and HIV Dementia Scale (HDS; Power, Selnes, Grim, & McArthur, 1995) are thought to be lacking in sensitivity for HIV related cognitive deficits even when they progress to become ADC (Carey et al., 2004; Smith et al., 2003). The recommendations of the 1989 NIMH Workshop recommended that for brief screenings neuropsychologists assess the following areas: premorbid intelligence, memory, processing speed and attention, depression, and anxiety (Butters et al., 1990).

In 1987, Ayers, Abrams, Newell, and Friedrich concluded that HIV+ individuals' neuropsychological responses using the Luria-Nebraska Neuropsychological Battery (LNNB; Golden, Hammeke, & Purisch, 1978) contained significant inconsistencies and were difficult to categorize by cognitive symptoms alone. Although patients are likely to perform differently on

cognitive measures, depending on medical HIV stage, there does not appear to be adequate information about the relationship between stages of disease and performance on specific neuropsychological measures. This appears to be a deficit within the literature. Ultimately, neuropsychological testing for ADC will provide more accurate prediction of prognosis, screen for deficiencies that may interfere with medication/medical regimen adherence, and identify those in need of intervention (Davis et al., 2002).

Summary and Study Aim

Dementia due to HIV is a disorder that has begun to receive more attention from clinicians and researchers. Advancements in identification and medical treatments for HIV have allowed patients infected with HIV to live longer, more productive lives. This has afforded researchers more time and resources to investigate the neuropsychological effects of this disorder. However, given that individuals with HIV are living longer, they are more likely to experience cognitive decline, and thus clinicians will be treating more patients with dementia. This makes having a greater understanding of ADC even more important. If dementia can be considered a sign of HIV/AIDS progression, early detection of HIV-related dementia should be prioritized so that the appropriate medical and psychological interventions can be implemented (Butters et al., 1990).

The diagnosis of ADC is difficult to make for multiple reasons. First, outside of using criteria for dementia and indicating an etiology of HIV, there is limited information about the specific presentation of dementia due to HIV. That is, there is general information about the earliest stages and then the near-terminal markers of severe neuropsychological impairment (Buckingham & Van Gorp, 1988) with minimal information about clinical progression of ADC. Specifics regarding neuropsychological performance at the various stages of the disorder are

lacking within the literature and commonly indicate only that the disease progresses into more advanced stages (Navia, 1990).

Secondly, biological markers do not show consistent significant correlations with neuropsychological performance. There does not appear to be research that examines performance on specific tests (i.e. the examination of localization and brain functioning) for the purpose of outlining a progressive profile for patients suffering from HIV-related cognitive decline. Thirdly, as there is no noninvasive marker to monitor the progression and severity of HIV-related dementia (Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999) other "nontraditional" markers should be explored. Prior studies have looked at the impact of severity of disease from an asymptomatic/symptomatic perspective (Tross, 1990), and others have examined the relationship between dementia and biological markers. However, none to date have included both markers (i.e. stage of disease with CD4 count: De Ronchi et al., 2002). This appears to be a deficit within the literature and an impediment to our understanding of the condition.

Thus, while research in the past two decades has greatly added to the knowledge base surrounding ADC, and influenced treatment practices accordingly, there are many areas that are unexplored or require further investigation. Given the lengthening life span of this population, the likelihood that they will experience and recognize cognitive declines grows, requiring psychologists to better understand, diagnose, and treat greater numbers of people with ADC. Prior literature has failed to explain HIV-related dementia in such a manner that cognitive declines can be directly correlated with health status or predicted by known biological markers of health status.

In addition, as mentioned earlier, the current research has addressed the neuropsychological functioning in patients in the initial stages of ADC. It is understood that not all patients within the earlier stages of HIV/AIDS experience cognitive impairments. Those with more impairment than their non-HIV+ counterparts are more likely to have subclinical cognitive decline as opposed to a diagnosable dementia. Therefore, these individuals may not be the best candidates from which to gain more in-depth information regarding the clinical presentation of ADC while examining health status. Along those lines, individuals in the later stages of HIV/AIDS are subject to more pervasive neuropsychological dysfunction. Therefore they may not be the best subpopulation to gather exploratory data from, as they are likely to show impairment across most areas of neuropsychological functioning. It is those individuals that could be considered in the "middle stages" of the disease that may be the best candidates for the current study, as a greater portion of this subpopulation (as compared to those in the earlier stages of the disease) is at risk for cognitive impairment. From an applied perspective, this middle group may yield the greatest benefit from exploration as the extent of their impairments may not be so severe as to exclude them from a positive outcome resulting from cognitive, behavioral, and pharmacological intervention.

The purpose of the present study was to provide an exploratory examination of the neuropsychological profile of individuals with HIV/AIDS. This research is important because HIV/AIDS is a devastating disease associated with both physical and mental declines. In addition, data were collected from patients seeking medical services from a charity hospital in the southern US, which also takes into account that many of the barriers that face low SES patients living with HIV/AIDS including poor appointment attendance and medical regimen nonadherence. Richardson et al. (2005) suggest that sampling patients within minority

populations (e.g. race, psychiatric illness, substance abuse) is important as the "sample represents a significant minority of the US population of adults living with HIV disease- particularly in large urban settings". Researchers have found that Blacks, when grouped by CD4 count, showed significantly lower viral load than a sample of Caucasians similarly grouped (Smith et al., 2003). These authors also found no significant differences in disease progression in these two groups but suggested that "ethnic differences are greatest during the early stages of HIV infection". While there currently does not appear to be literature examining the neuropsychological progression of ADC in a predominantly African-American population, there is evidence that individuals of African descent present for treatment with more progressed disease, have less opportunity to benefit from antiretroviral therapy, and thus have not experienced reduction in mortality rates found in other populations with HIV/AIDS (Boyd et al., 2005), which likely places them at greater risk of experiencing ADC. In addition, the CDC (2005) reports that African Americans currently comprise 49% of newly diagnosed cases of HIV, which also highlights the importance of conducting more research with this population. The current study intends to provide more information about neuropsychological impairment in this population.

Acquiring more information about the progression of neuropsychological decline in this population will also highlight issues pertaining to quality of life and possibly prediction for declines, which will help physicians and patients prepare for possible cognitive impairment and guide medical and behavioral modifications necessary to prevent substantial declines in quality of life. In a study using predominantly male, African American subjects conducted at the Medical Center of Louisiana in New Orleans (MCLNO), the authors reported that acquiring dementia, amongst other HIV-related medical problems, is associated with decreases in life expectancy (Welch, Morse, & Adult Spectrum of Disease Project, 2002). The researchers

suggest that because of new medical advancements (e.g., HAART), individuals with HIV/AIDS are living longer and thus more information is needed about the neurological conditions that contribute to decreased survival. Lastly, as patients are living longer with HIV/AIDS, it is likely that we will continue to see increases in the number of patients with cognitive decline and HIV-related dementia. Having more information about the symptoms associated with stage of disease may also assist clinicians by providing treatment recommendations that will minimize the progression of neuropsychological decline and thus minimize patient suffering in this population.

In the current study, patients were selected based on their HIV+ status. People who were symptomatic with infection, but did not have an AIDS indicator condition, were eligible for participation. Initially this project intended to group participants into one of three categories based on their t-cell count. That is, this study sought to examine the neuropsychological profile of group B (see Appendix A for information on HIV+ health status); those considered in "the middle stages" of HIV/AIDS. However, due to difficulties obtaining adequate samples from each of the three groups, participants were grouped into one of two groups (G1 and G2), based on their t-cell count. As noted previously, this is an understudied subpopulation of HIV/AIDS patients, and may be important in providing information about the trajectory of cognitive decline. Those meeting criteria for participation in this study were given a neuropsychological battery to specifically investigate the nature and severity of impairment. Chart reviews provided information regarding biological markers.

Hypotheses

1. It was hypothesized that patients with more severe HIV-related health problems (as assessed by t-cell count within the health severity framework within HIV symptomatic individuals) would show greater cognitive related impairments.

2. It was hypothesized that health severity groups would differ in neuropsychological profile (across areas of functioning) (e.g. motor, learning, etc.) depending on their current HIV-related health status. Given lack of research in this area, no specific profile patterns were proposed, but it was suspected that patients who are experiencing more significant HIV related health symptoms would have more impaired neuropsychological functioning.

Methods

Participants

Patients diagnosed with HIV/AIDS were approached in the waiting room of the Early

Intervention Clinic (EIC) at Earl K. Long Medical Center for participation in this study. The

EIC is a HIV/AIDS specialty clinic within the Earl K. Long Medical Center, which serves low

SES, predominantly African-American individuals. Only patients with HIV/AIDS are treated at

EIC and therefore patients did not require screening for HIV/AIDS status. Patients were

excluded from this study if they had been diagnosed with HIV/AIDS for less than 6 months or

were less than 18 years of age. Patients were also excluded if they have not had blood work (i.e.

updated information about CD4 count and viral load) completed in the past 9 months. Patients

were excluded if they belonged in categories A or C according to the table in Appendix A.

Data were available on enrollment rates for 50 clinics representing a small sample from

this 9 month study. In addition, data were gathered for patients that were scheduled for an

appointment for each of the 50 clinics that did not show up for their visit. Including the no

shows, 108 potential participants were eligible for this study during those 50 clinics. No shows

accounted for 42.6% (46 people), 11.1% (12 people) were not interested in participating, 30.6%

(33 people) were tested, and 15.7% (17 people) were not tested for other reasons (9 were missed

while examiner was testing another patient, 3 discontinued testing, 3 had already been tested, 1

was not recruited due to examiner illness, and 1 agreed to participate and was found to be

ineligible for participation). A total of 55 subjects participated in this study.

The high no show rate in this study appears to be lower than findings from prior research

conducted at EIC at the Earl K. Long Medical Center. Johnson (2002) found that the average

attendance (defined by attending 80% of one's schedule appointments over a one year period)

rate for individuals was 71% and was negatively correlated with t-cell count and minority status, which may explain the lower attendance rates during the current study as participants were symptomatic with HIV infection and a predominantly minority sample.

Procedure

Informed consent was obtained from individuals willing to participate, and the investigator reviewed their medical records to ensure that they met criteria for participation in this study (i.e., symptomatic infection). The consent form (see Appendix B) contained information about confidentiality, the procedure of this study, potential harm to the patient (minimal) and conforms to criteria established by the National Institute of Mental Health. It also indicated that information will be collected about them from their medical chart. Potential participants were provided with contact information should they have further questions or if they would like to know the results of the study. Once the patient's informed consent was obtained, they followed the investigator to an examination room where the testing was conducted.

To address potential problems or difficulties with reading, all measures were administered to the patient by the investigator. The first measure that was administered was the BDI-II. If the client endorsed a 1 or more on item 9 (suicidality) or achieved a total score of 29 or higher, a thorough suicide assessment would have been conducted with the patient. No patients were found to be at risk for causing harm to themselves or another person, and thus no follow-up was necessary. Two patients who endorsed significant depressive symptoms without suicidal/homicidal ideation were referred to psychology services for further assessment.

Following administration of the BDI-II, the rest of the test battery was administered. Test administration took from 45 to 90 minutes. A small edible incentive was offered for participation in this study (their choice out of a multi-pack of chips or a small fruit juice box). In

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addition, those that completed the entire battery were given a $15 gift certificate to Wal-Mart. All data were collected by a graduate student in neuropsychology in the doctoral clinical psychology program at Louisiana State University, and trained research assistants.

Measures

Demographic Questionnaire. A demographic questionnaire was completed (see Appendix C) to obtain psychosocial and basic medical information. The following information was collected from the patient's chart: hospital number, t-cell count, viral load, HIV-severity (clearly indicated on physician medical chart note), and current medications.

Neuropsychological Battery. While using multiple dependant variables can lead to problems with adequate power, it was decided that the neuropsychological battery would be chosen based on what measures most comprehensively assessed functioning across cognitive domains to fully explore stated hypotheses. The specific tests included in the present study were selected by 1) ability to assess multiple areas of cognitive functioning while still maintaining brevity in assessment time, 2) consistency with existing studies in the HIV dementia literature (Chang, Ernst, Witt, Ames, Gaiefsky, & Miller, 2002; Everall, 1995), and 3) ability to assess cognitive domains commonly believed to be effected by the HIV virus. While the number of assessment measures of HIV-related dementia continue to increase, the traditional neuropsychological measures (e.g., the Halstead-Reitan) are still considered to be the most successful for identifying cognitively impaired patients (Gonzalez, 2003). The comprehensive battery included the following tests which took 45-90 minutes to complete. Tests were chosen and administered in the order they were administered to decrease testing time and ensure the best possible transition between measures.

The Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) is a 21 question self-report measure of assessing the severity of depressive symptoms. The BDI-II has been deemed reliable and valid in a variety of settings, including primary care, where it has been found to achieve internal consistency of .94 and strong factorial validity (Arnau, Meagher, Norris, & Bramson, 2001). Total raw scores were used to analyze group comparisons.

The Rey Complex Figure Test (RCFT; Rey, 1941) assesses visual-spatial ability and visual memory. This test includes copy, immediate recall and delayed recall drawing trials. During the copy trial, the subject is able to copy a figure onto a blank piece of paper. The stimulus is removed following this trial and the immediate recall occurs as the individual is asked to recreate the drawing to the best of their abilities. The delay recall occurs at least 10-15 minutes after the immediate recall. This measure is widely used to measure perceptual organization as well as visual memory (Fastenau, Denburg, & Hufford, 1999) and is reported to have high reliability ranging from .93 to .97 (Deckersbach et al., 2000). For this study, t-scores were examined for the delay and immediate tasks.

The State Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) is a 40 item self-report questionnaire that assesses both state and trait anxiety levels. State anxiety is thought to fluctuate depending on one's situation, and trait anxiety refers to anxiety that is relatively stable (Rule & Traver, 1983). Rule and Traver found that across a two-week period reliability for state was .40 and for trait was .86. State and trait t-scores were evaluated for this study.

The California Verbal Learning Test-Second Edition Short Version (CVLT-II; Delis, Kramer, Kalpan, & Ober, 2000) assesses verbal learning and memory by requiring subjects to recall a list of words presented verbally over a series of trials. The participant is read a list of

words four times, after each trial he/she is asked to recall as many words as possible. A distractor task is completed followed by which the individual is asked to recall as many words as possible (short-delay free recall). There is a 10-minute delay until the long-delay free recall. Next, the individual is given the long-delay cued recall, where he/she is asked to produce words from the list by subject (i.e. fruits, clothing, and tools). The final subtest is the yes/no recognition where the subject is required to respond to whether or not they think certain words were on the list. According to Donders (2006), the CVLT-II has "acceptable" reliability, ranging from .78-.94. The trials 1-4 t-scores and learning slope standard scores were evaluated for this study.

Grooved Pegboard (Klove, 1963, Matthews and Klove, 1964) assesses fine motor skills and coordination. This measure consists of a small board with 25 holes for peg placement to be placed as quickly as possible. The subject attempts this task with their dominant hand and then their non-dominant hand. Reliability has been reported as .80 (dominant hand) and .81 (non-dominant hand) for completion time (Knights and Moule, 1968). Mahurin and Inbody (1989) reported that grooved pegboard was a valid measure of visual-motor coordination. Dominant and non-dominant t-scores were analyzed in this study.

Trail Making A and B (TMT; Partington & Leiter, 1949) assesses attention, scanning, processing speed and sequential problem solving. This measure requires individuals to quickly scan and draw connecting lines between consecutive numbers in part A. For part B, cognitive flexibility is used to alternate between numbers and letters for rapid sequencing. While this is one of the most widely used instruments in neuropsychological assessment, the original TMT does not have well-normed psychometrics representative of the current population (Reynolds, 2004). T-scores for parts A and B were evaluated in the current research.

The North American Adult Reading Test (NAART; Blair & Spreen, 1989) is a brief screener used to assess for verbal intellectual ability. Subjects are asked to read aloud from a list of words. The reliability of the NAART is .93, and the validity coefficient is .75 (Uttl, 2002). This test consists of 61 irregular words and is scored for accuracy according to American rules and correlates with the WAIS-R Verbal IQ, Performance IQ, and Full Scale IQ (Uttl, 2002). For this study, results from the full scale IQ calculations were used.

The Controlled Oral Word Association Test (COWAT: FAS; Benton and Hamsher, 1976; Benton, Hamsher, & Sivan., 1983) assesses verbal fluency and spontaneity by requiring oral production of spoken words. Three letters (F, A, and S) are identified and the participant is asked to name as many words as possible beginning with that letter in one minute. While considered to have good interrater reliability (r=.9), (Ross et al., 2007), normative data for individuals with IQ scores that are below average are not currently available (Loonstra, Tarlow, & Sellers, 2001). The COWAT has also achieved test-retest reliability of .84 (Ross et al., 2007). T-scores derived from the FAS total score were used in analyses in this study.

The Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983) is a 60-item measure that assesses language and naming by requiring subjects to identify objects presented via ink drawings with varying levels of familiarity. Stimulus cues are provided when subjects are unable to identify objects to examine the usefulness of verbal prompting. If the subject does not identify the item following a stimulus cue, a phonemic cue is provided. The BNT is one of the most commonly used language measures, and is strongly correlated with reading vocabulary and less correlated with psychiatric diagnosis, age (Hawkins et al., 1993), and gender (Heaton, Avitable, Grant, & Matthews, 1999). Hawkins et al. report that subjects with lower reading

ability are at greater risk of misdiagnosis according to their total score on the BNT. T-scores converted from the total score were used for analyses in this study.

The Stroop Color Interference Test (Stroop, 1935) assesses executive functioning, attention, and concentration by asking participants to utilize cognitive flexibility as they read words without interference from the colors that they are presented in and vice versa. First, subjects are timed while they read a list of words with colors on them. During the second task, a page with 100 XXXX's are shown, each XXXX is in a different color and the individual is asked to report the color as quickly as possible. Lastly, the individual is show a list of colors, but the color of ink does not match the color that the list says, and the subject is asked to report the color of the ink as opposed to stating which color is written. Reliabilities have been reported to range from .73-.86 (Roybal, 2004). Information from the color-word t-score was used in analyses for this study.

Within each patient's medical chart, data is available regarding the patient's clinical health status. This information includes information about the patient's t-cell count as well as their HIV-related health status. This "clinical classification" groups patients into one of nine cells (see Appendix A for more information and an illustration of this chart).

Independent Variables

1. Demographic variables: Demographic variables will be obtained from each of the participants. These include age, race, years of education, number of years diagnosed with HIV/AIDS, and gender. We also examined demographic variables for suitability for covariates

2. Health status: Information about the patients' health status was obtained through chart reviews (i.e., t-cell count and HIV-related symptoms) by gathering information

about their "health classification". The early intervention clinic uses physician intake

forms which will aid the ease with which this health information is acquired.

Physician intake forms clearly identify the client's t-cell count, viral load, and health

status (i.e., B1, B2, B3). T-cell count and health status were used to determine

initially which group participants were in (i.e., B1, B2, or B3) for purposes of this

study and were later recoded and collapsed into two variables (G1 and G2; refer to

Appendix A for illustration of health status classification chart and new groupings).

Dependent Variables

The dependent variables (DV) are the results of neuropsychological testing in each of

the domains of functioning. For example, the patients' scores on measures of

language, motor, memory, intelligence, etc.

Sample Size and Analyses

For this exploratory project intended to have three cells of data, a total of 60 subjects with

completed information were desired, and a total of 59 subjects were successfully recruited and

55 subjects successfully completed the test battery.

Descriptive data were analyzed for all subjects. Although three groups were intended for

analyses, subjects were regrouped into one of two groups. As performance was expected to be

higher in Group 1 than Group 2, one-tailed, independent samples t-tests were run to analyze

differences in group means. Analyses were also run that controlled for variables that may have a

strong association with the dependant variable.

Additionally, strength of association tests were calculated to assess the variance in the

performance measures that is associated with the two groups. To assess how much of an

association exists, partial eta squared ($\eta^2 p$) was calculated. This statistic was chosen because

findings are less sensitive to the number and significance levels of the other groups in the design. Partial eta squared also allows for estimations about the proportion of variance in the greater population (Tabachnick & Fidell, 2001). For this study, effect sizes were measured by Cohen's (1988) guidelines: small effect = .01, medium effect = .06, and a large effect = .14.

Group means were also used to examine the neuropsychological profiles of the two groups according to t-test classification ranges. These classification ranges allowed the researcher to better describe the overall neuropsychological profile of the two groups by placing them in categories that reflect general functioning (e.g. above average, average, below average, etc.). In addition, this classification provided information about the performance in each cognitive domain relative to the others.

Additional analyses were conducted to examine the relationships between dependent variables and predictor variables. Separate backward selection multiple linear regressions were run for each of the neuropsychological tests, using recent viral load, race, age, number of years diagnosed, highest level of education achieved, and recent CD4 count as predictors. Backward selection was used to reveal the smallest set of predictors that explain the most variance. As there were no hypotheses made about the variances in predictors and these analyses were exploratory, other models were deemed less appropriate (e.g. hierarchical).

Results

Descriptive Data

Of the 55 participants, roughly half were female (50.9%), and the majority were African-American (85.5%), unemployed (78.2%), and had never married (47.3%). Married participants comprised 14.5% of the sample, with 7.3% separated, 16.4% divorced, and 14.5% widowed. Alcohol use in the past week was reported by 16.4%, and 9.1% endorsed recent drug use. The mean age was 44.89 years, and the sample averaged 11.93 years in education.

The average number of years diagnosed for the 55 participants was 8.25. The average CD4 count was 488.98, and the average Viral Load was 53,903.08. Two participants did not have recent Viral Load information in their medical records and thus, were excluded from viral load descriptive analysis.

The sample fell into the following categories based on physician categorization from the participant's chart: 3 B1s (5.5%), 13 B2s (23.6%) and 39 (70.9%) B3s. CD4 count was examined between the three health classification groups as well. Results showed no significant differences for CD4 count between the three groups, $F(2, 52) = 0.825$, $p = .44$. These results are surprising because within the B health classification system, the three groups are determined by their CD4 count. Thus, one would expect to see significant differences in CD4 count between groups. The data were re-examined and, for many of the subjects ($n = 36$), the reported health classification did not correspond to the most recent CD4 count acquired from patients' medical records. A new variable was created that reclassified patients into one of the three categories based on CD4 count. For the purposes of this paper, this reclassification will be referred to as Kendra classification. Following reclassification, frequencies within the three groups became: 29 B1s (52.7%), 14 B2s = (25.5%), and 12 B3s = (21.8%). Analysis of mean CD4 count under the

Kendra classification showed significant differences between the three groups, $F(2,52) =$ 92.401, $p < .001$. As these regroupings were much different than the physician-designated groupings, the validity and reliability of using these three categories was questionable. It seemed more appropriate to group by CD4 count alone because the lab data seemed more reliable for group comparisons.

Due to concerns of generalizability from small cell sizes and the inconsistent health categorization data, new groupings were created. Based on median CD4 count, the cutoff between the two groups was placed at 500. Thus the new groups became Group 1 (G1) which included all subjects with a CD4 count of 500 or above (which was previously the B1 group) and Group 2 (G2), which included all subjects that had a CD4 count lower than 500 (formerly groups B2 and B3). Under this new grouping, CD4 count between the two groups were significantly different, $t(53) = 11.404$, $p < .001$. Refer to table 1 for illustration of the three groupings.

Table 1

Patient groupings.

First Grouping	Second Grouping (Kendra Classification)	Final Grouping
B1 $N = 3$	B1 $N = 29$	G1 $N = 29$
B2 $N = 13$	B2 $N = 14$	G2 $N = 26$
B3 $N = 39$	B3 $N = 12$	

Note: Final Grouping was used in data analysis for this study.

The two new groups had sample sizes that were much more comparable. G1 consisted of 29 subjects (52.7%) and G2 had 26 subjects (47.3%). No significant differences were found between groups for marital status distribution, $\chi^2(1, N = 55) = 4.58$, $p = .334$, gender distribution $\chi^2(1, N = 55) = 0.016$, $p = .90$, or race, Fisher's Exact, $p = .054$, with only one Caucasian

participant included in G2. Two-tailed *t*-tests revealed no significant differences between groups

for years diagnosed, $t(53) = 1.42, p = .160$, or age, $t(53) = .477, p = .64$. The two groups differed

significantly for highest education level obtained, $t(53) = 2.341, p = .02$. It is noteworthy that the

standard deviations for CD4 count were very high, indicating that the group means are not the

most accurate representation of the data. This is likely because the three groups were dissolved

into two groups, which included a larger range of CD4 counts in each group. The same is true

for the standard deviations for viral load. See Table 2 for demographic information by health

status groups.

Table 2

Demographics for G1 and G2

Variables	G1 *N* =29	%	SD	G2 *N* =26	%	SD
Age	*M* = 45.52		10.84	*M* = 44.19		9.63
Education (years)	*M* = 12.45		1.55	*M* = 11.35		1.92
Years Diagnosed	*M* = 9.24		5.17	*M* = 7.15		5.70
Gender						
Male	*n* = 14	48.3%		*n* = 13	50%	
Female	*n* = 15	51.7%		*n* = 13	50%	
Marital Status						
Single	*n* = 15	51.7%		*n* = 11	42.3%	
Married	*n* = 2	6.9%		*n* = 6	23.1%	
Separated	*n* = 2	6.9%		*n* = 2	7.7%	
Divorced	*n* = 4	13.8%		*n* = 5	19.2%	
Widowed	*n* = 6	20.7%		*n* = 2	7.7%	
Race						
White	*n* = 7	24.1%		*n* = 1	3.8%	
Black	*n* = 22	75.9%		*n* = 25	96.2%	
Recent CD4 Count	*M* = 713.97		169.47	*M* = 238.04		135.84
Recent Viral Load	*M* = 13226.36		40284.35	*M* = 99461.00		242302.6

Analyses of Group Differences

Mood. On the BDI-II, both G1 ($M = 14.97$) and G2 ($M =11.54$) were, on average, within

the Mildly Depressed range, with no significant differences between groups, $t(53) = 1.002, p =$

.16, $\eta^2 p = .019$. On the STAI, no significant differences were found between groups for state

anxiety, t (53) = .118, p = .45, $\eta^2 p$ < .001, or trait anxiety, t (53) = .181, p = .43, $\eta^2 p$ = .001. The

means for G1 and G2 for state anxiety (60.76 and 60.54 respectively) placed them both within

the Borderline Elevated range. For trait anxiety, means (G1: M = 65.10, Significantly Elevated

range; G2: M = 64.77, Borderline Elevated range) were higher than state anxiety means. BDI-II

scores were included as covariates on all further analyses. The BDI showed a significant effect (p

= .03) on memory, but no other measures appeared to have significant effects of depression

and/or anxiety.

 Intellectual Ability. On the NAART full scale IQ (FSIQ), the two groups were not

significantly different, t (50) = .943 p = .18, $\eta^2 p$ = .017. The group mean for G1 was 98.39 and

for G2 was 95.49 indicating FSIQs within the Average range. For comparisons of classification

ranges across this and other cognitive domains see Figure 1.

 Motor and Coordination Task. On the grooved pegboard, no significant differences

between groups were found for dominant hand, t (53) = -0.063, p = .48, $\eta^2 p$ =< .001, or

nondominant hand, t (51) = -0.159, p = .44, $\eta^2 p$ =< .001. For dominant hand, both groups

averaged t-scores of 41.0, placing them in the Below Average range. On the nondominant hand,

groups scores averaged 44.17 (G1) and 44.75 (G2), which placed them in the Below Average

range as well.

 Attention and Processing Speed. On the TMT Part A, no significant differences between

groups were found t (53) = -0.455, p = .33, $\eta^2 p$ = .004. The mean for G1 was 42.14 and was

43.62 for G2, which placed them in the Below Average range. Likewise, no significant

differences between groups were found on TMT Part B, t (53) = -0.442, p = .33, $\eta^2 p$ = .004.

G1's average t-score was 45.34 and G2's average t-score was 46.69, which placed both groups in

the Average range on this measure.

Concentration and Executive Functioning. On the Stroop task, no significant differences between groups were found for the color-word trial, t (53) = 0.129, p = .45, $\eta^2 p$ < .001. While controlling for race (p = .99), years of education (p = .75), and FSIQ (p = .005), no significant differences were present between groups on the color-word trial (mean t-score for both groups was 37.0, Mildly Impaired range), $F(1,53)$ = .08, p = .78.

Memory and Learning. On the CVLT-II t-scores between the two groups were not significantly different, t (53) = 1.439, p = .08, $\eta^2 p$ = .038 for memory. While controlling for years of education, (p = .014), FSIQ (p = .023), and age (p = .008) there was no effect of group status on memory $F(1,47)$ = .353, p = .56. The mean for G1 was 41.86, which placed them in the Below Average range, and the mean for G2 was 37.23, which placed them in the Mildly Impaired range. No significant differences were found between groups on a measure of learning, t (53) = -0.463, p = .32, $\eta^2 p$ = .004.

Visual-spatial Ability and Visual Memory. On the Rey Complex Figure Test, the two groups were significantly different on the immediate task, t (53) = 1.76, p = .042, $\eta^2 p$ = .055, as well as the delayed task, t (53) = 2.060, p = .02, $\eta^2 p$ = .071. On the immediate task, G1 placed in the Mildly Impaired Range (M = 35.38) and G2 placed in the Moderately Impaired range (M = 28.92). On the delayed task, G1 scored an average of 33.55, which placed them in the Mildly to Moderately Impaired range, and G2 scored an average of 26.62 which placed them in the Moderately Impaired range. While controlling for number of years of education (p = .41), race (p = .14), or age (p = .29) no significant differences were present between groups $F(1,54)$ = 1.61, p = .21 on the delayed task.

Language. On the Boston Naming Test, the two groups were not significantly different, t (48) = .536, p = .30, $\eta^2 p$ = .006, and results did not change when age, race, education, or FSIQ

were included as covariates. G1 and G2 placed in the Below Average range on this measure ($M =$ 42.07 and 40.00, respectively).

Verbal Fluency. On the Controlled Oral Word Association Test, no significant differences were found between groups, $t(51) = .038$, $p = .49$, $\eta^2 p < .001$, and results did not change when age, race, education, or FSIQ were included as covariates. According to classification ranges, both groups scored in the Below Average range (G1, $M = 42.64$; G2, $M =$ 42.52).
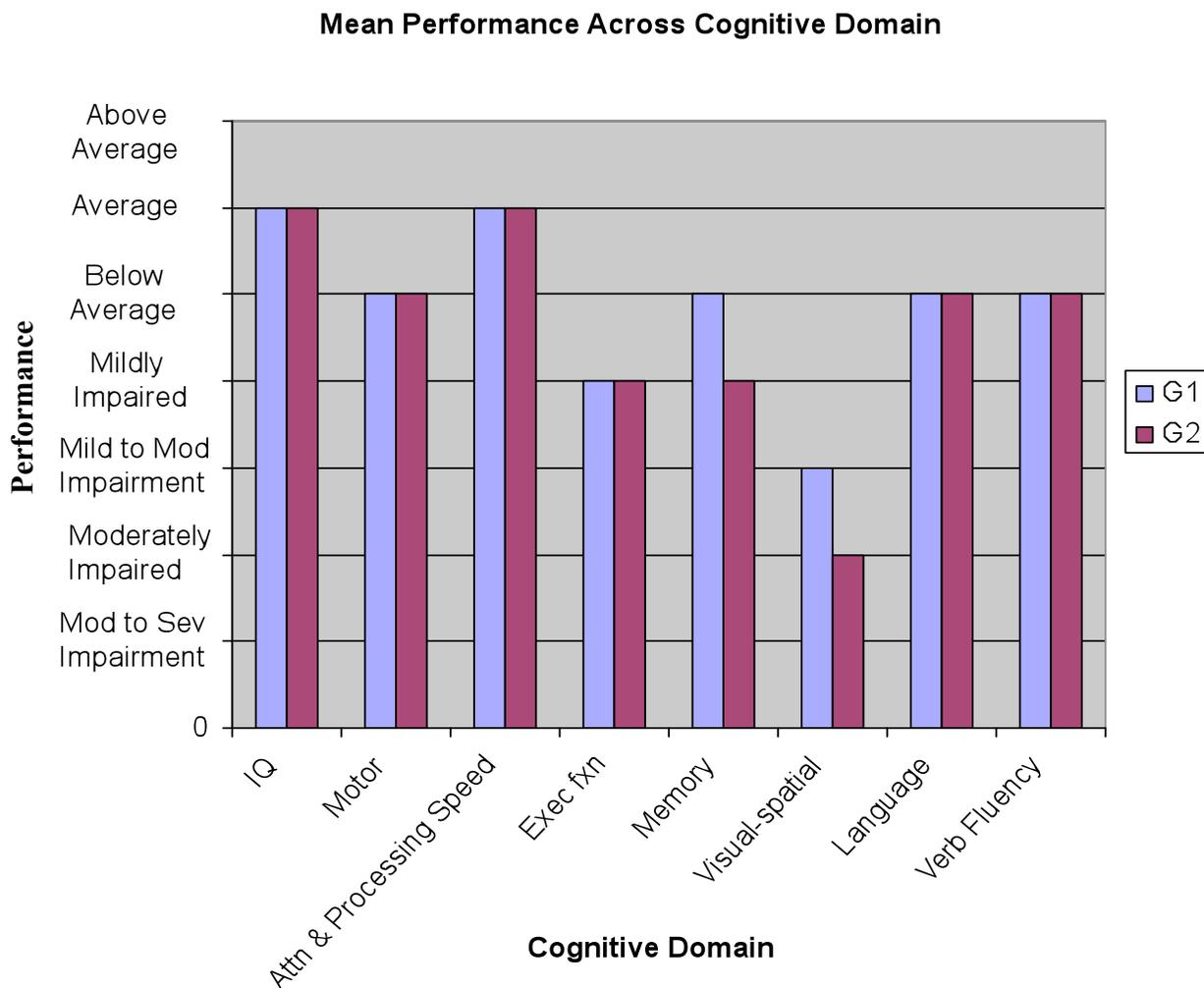

Figure 1. Mean performances for G1 and G2 for each cognitive domain

Additional Analyses

As visual-spatial ability and memory were the only variables in which G1 and G2 differed, follow-up analyses were conducted to examine the relationships between dependent and independent variables. Separate backward selection multiple linear regressions were run for each of the neuropsychological tests, using recent viral load, race, age, number of years diagnosed, highest level of education achieved, and recent CD4 count as predictors.

Intellectual Ability. Using the backward method with FSIQ as the dependant variable, the final model included the significant predictors, years of education ($\beta = 0.296$, $p = .025$) and race ($\beta = -0.3.68$, $p = .0006$), $F(2, 47) = 8.452$, $p = .001$, Adjusted $R^2 = .233$.

Memory and Learning. Using the backward method with the CVLT-II as the dependant variable, the final model included the significant predictors, years of education ($\beta = 0.371$, $p = .003$) and age ($\beta = 2.89$, $p = .017$), $F(3, 49) = 8.860$, $p < .001$, Adjusted $R^2 = .312$ on the trials memory task.

Motor and Coordination. Using the backward method with the grooved pegboard (dominant hand) as the dependant variable, the final model included the significant predictor, age ($\beta = -.333$, $p = .015$), $F(1, 51) = 6.364$, $p = .015$, Adjusted $R^2 = .092$.

Visual-spatial Ability and Memory. Using the backward method with the delay task on the RCFT as the dependent variable, the final model included the significant predictor, race ($\beta = -.269$, $p = .047$), $F(3, 49) = 3.878$, $p = .014$, Adjusted $R^2 = .142$.

Significant models using the above predictor set did not emerge for learning, $F(1, 52) = .413$, $p = .52$, concentration and executive function, $F(1, 51) = 2.257$, $p = .139$, attention and processing speed (Trails Part B), $F(1, 51) = 2.025$, $p = .161$, language, $F(1, 46) = 2.365$, $p = .131$, and verbal fluency $F(1, 49) = 1.045$, $p = .312$.

Discussion

Group Identification

      An initial problem with analyzing these data was identifying comparison groups. It is still unclear why the physician-determined group appears to differ from the group using CD4 count (Kendra classification) alone for categorization. This could be due to physician failure to update the classification despite receiving new lab work reflecting current CD4 count. One consideration that should be explored in future research is whether there may be some patient-care advantage in not reclassifying patients. That is, there might be treatment gains or greater medical cost coverage provided for patients with more or less advanced HIV or stabilized medical conditions. This may be difficult to assess, but would provide information about rationale for physician decision to not update or reclassify patient health information. There may also be a medical reason for not reclassifying patients even if their CD4 count changes which is not readily found in the literature. This information will be essential for future research using physician report and biological data with this population.

      Regardless of why the discrepancy in classification occurred, when classified into three groups, one of the three groups had significantly fewer patients enrolled in the study. Initially it appeared that it was the B1s that were not attending clinic appointments and thus were unavailable to participate in this study. That being the case, it is possible that HIV+ individuals that are relatively healthy may be less motivated to attend clinic appointments because they do not believe that their condition is severe enough to warrant intensive medical care. Another possibility is that, as comparing group means suggests, this group has more members that are more recently diagnosed or new to the clinic, they may lack the education about the importance

of adherence and may still be dealing with stressors related to adjusting to their diagnosis, which could also interfere with clinic attendance.

When looking at the regrouping only by CD4 count (Kendra classification), it appeared that the clinic attendees with the highest no-show rates were the B3s. Considering this information, it could be that B3s are the most nonadherent group in the B category, which would also contribute to their worsened health condition. Another explanation is that this group is receiving more acute care (e.g., hospitalizations and other specialty clinics) because of illness severity, and is not attending outpatient clinics. Another hypothesis is that this group experiences the highest level of health related frustration and hopelessness and has thus lost motivation for medical regimen adherence including clinic attendance.

Ultimately, it seemed most methodologically sound to condense the three groups into two groups by CD4 count. This researcher had greater confidence in the lab work than in overriding the physicians' designation and using a self-determined one (Kendra classification). As a result of using two groups instead of three, there was a deviation from the health classification system that this project was based on. While these results were useful in determining the extent, or lack thereof, that neuropsychological impairment differs in groups based on CD4 count, these findings cannot sufficiently support or reject the use of this health classification system in the evaluation of neuropsychological impairment in individuals with HIV/AIDS in category B.

Hypothesis #1

The first hypothesis that patients with more severe HIV-related health problems would show greater cognitive-related impairments was not statistically supported by this research which compared means and examined effect sizes. The only domain where there was a significant difference between groups was on the immediate and delayed tasks of the Rey Complex Figure

Test measuring visual-spatial skills. This finding is interesting because impaired performance in visual memory and visual-spatial performance is usually found in the later stages of ADC (Field, 1993; Navia, 1990). However, looking at group means and classification ranges across cognitive domains, generally speaking, these profiles are not representative of profiles suggesting later stages of ADC. Effect sizes also supported these findings, revealing that only the memory and visual-spatial tasks showing medium sized effects, with all other variables resulting in small effect sizes. It is possible that such small effect sizes for the majority of the measures reflects a sample size that is too small for group differences and effects to be identified.

The effect that mood symptoms may be having on neuropsychological functioning was also investigated, but was not significant. Perhaps no significant effect was found because most individuals in the B category have a similar neuropsychological profile regardless of CD4 count. Additionally, it could be that given the similar health status, patients are at similar mood levels despite any variance in CD4 count. Further research should explore the effects that mood exerts on neuropsychological functioning.

Narrowing the range of subjects to category B was possibly too restrictive to find group differences. Because patients in each of the categories share similar HIV-related health status it could be that they experience similar neuropsychological levels of functioning. Should that be the case, it is likely that group differences would be found between groups as defined by group classification (i.e. A, B, and C). The current study sought to examine group B because they may be viewed as the "middle of the road" HIV/AIDS patients. Therefore it was thought that this would be the best sample to start with because they were the most likely to have neuropsychological impairment without being significantly impaired across all domains. Given that it is clear that there are differences in neuropsychological performance between patients

asymptomatic and patients in the end stage of the disease, those groups were excluded from this study in an effort to test this model more closely. However, given the current findings, it may be necessary to investigate the group differences between categories A and C. Those findings could then be used to see if there is a solid foundation for continuing to evaluate this health classification as an effective model for examining neuropsychological impairment. If there is no group difference found between A1 and C3, we can assume that this is not a useful framework. Future research could also investigate differences between the A, B, and C categories to see if the health status has a greater predictive value than CD4 count alone. That is, because this study looked at the category B alone, group differences by CD4 count were explored. Patients with differing medical status were not compared and thus no report can be made about the effect of differing medical condition on neuropsychological functioning. However, looking at all nine possible cells would highlight the group differences as defined by health status and CD4 count.

Hypothesis #2

The second hypothesis was that health severity groups would differ in neuropsychological profile across areas of functioning depending on their current HIV-related health status. While looking at these classification ranges does not necessarily have statistical implications, it is useful for assessing the overall profiles of performance and identifying strengths and weaknesses in neuropsychological performance. It should be noted that these profiles were gathered only from patients in group B, which might imply that profiles that are not significantly different means that individuals within the same health classification are experiencing very similar levels of neuropsychological functioning. What would be interesting about that finding would be the suggestion that health classification status is the primary predictor of neuropsychological functioning, above individual factors. Also, because the three

original groups were re-grouped into two groups, there may be less distinction in the profiles of the two groups.

No differences in classification ranges were found for depression, IQ, motor, attention and processing speed, concentration and executive functioning, language, or verbal fluency. For measures of memory and learning and visual-spatial skills, Group 1 performed better than Group 2 by one categorical placement (e.g. G1= below average, G2= mildly impaired). While group differences such as this could be expected in more cognitive domains, it is not surprising that G1 performed better than G2 on at least two measures. As early cognitive symptoms of ADC include slowness, impaired attention and concentration, and memory problems (Buckingham & Van Gorp, 1988; Navia, Jordan, and Price, 1986), it could be expected that both groups would have demonstrated greater impairment in attention and processing speed. It is interesting that the visual-spatial domain was the only area where patients presented with performance below mild impairment. Somewhat surprisingly, G1 was in the significantly elevated range for trait anxiety and G2 was borderline elevated. It could be that trait anxiety lends itself to higher levels of adherence and medical regimen conscientiousness due to health-related anxieties. Future studies may want to examine how anxieties, particularly health-related, impact neuropsychological performance in this population. Again, it is also possible that the neuropsychological profiles for patients in the B health classification group are similar regardless of CD4 count. Profiles for patients in all three groups (A, B, and C) should be explored and compared to see if it is the health status and not the CD4 count that has the greater impact on neuropsychological functioning.

Additional Investigation

Given the literature on psychosocial risk factors and progression of HIV-related dementia (Farinpour et al., 2003; Smith et al., 2003), it is interesting that demographic factors did not appear to have significant effect on neuropsychological performance. However, race, age, and years of education, although inconsistent predictors, appeared to have the greatest predictive values in terms of number of domains in which they were influential. It is somewhat surprising that the number of years diagnosed and viral load did not have predictive value of neuropsychological performance as they are both markers of health status. That is, neuropsychological impairment in patients with HIV/AIDS is better predicted by factors that are pre-existing and constant (e.g. race) than variables directly related to the medical condition (e.g. viral load).

Limitations

A primary limitation of this study is that, due to enrollment and group identification problems discussed previously, subjects had to be reclassified into one of two groups based on CD4 count. The author is aware that this, by definition, does not correspond exactly with the three groups in category B that this study set out to examine. Thus, these results have to be interpreted with caution in that the results do not directly reflect the validity of using this health classification system for identifying and treating neuropsychological impairment in this population.

As no baseline data were available for participants, it cannot be concluded that these results reflect the progression of HIV/AIDS. Future research may wish to use asymptomatic or non-HIV controls in a longitudinal study that investigates the progression of HIV and dementia symptoms over time. In addition, some of the data were self-report (e.g. drinking/drug use),

which may be unreliable. Included in this information is handedness, which should have been

tested in a more standardized manner to ensure appropriate test administration. Additionally, this

study did not consider the effects that certain medications may have had on the

neuropsychological functioning of patients at the time of testing.

In retrospect, testing patients while they were attending a clinic appointment may have

been a limitation. Not interfering with clinic procedures and the patients' appointment turned

out to be a greater challenge than originally expected. It may have been more ideal to test

patients, outside of the clinic to ensure that they would not be preoccupied or distracted by health

concerns or waiting for their appointment. However, it is very likely that it would have been

more difficult to recruit patients if they had to make a separate appointment. In some cases, the

testing appeared to serve as a distractor for the length of time that patients were waiting to see

their physician.

As with many studies that sample from clinic populations, generalizing to other samples

is made difficult by the implied medical regimen adherence among clinic attenders. That is, it

may be difficult to suggest that those that participated in this study will have the same profile as

those that did not attend clinic who may be less likely to take their medications/refill them,

abstain from maladaptive behaviors, and adhere to their medical regimen. Future research may

wish to include a broader sample. A recommended consideration would be to attempt to include

more Caucasians in a predominantly African-American sample. Because group 2 only had one

Caucasian participant, this study was not adequately able to compare the two groups by race.

Another issue that this study highlighted is the potential for group misclassification. As

this study was not equipped to fully explore the cause for the discrepancy from the outset, future

research should include a more detailed evaluation of the physician classification. The current

research was limited by having to shift from the initial proposal of comparing three groups as defined by health status to a comparison of two groups defined by CD4 count. While the difference may appear subtle, this study is unable to comment on the pros and cons of using the 3x3 health classification model, as initially planned.

In addition to the group misclassification, an unexpected limitation was the lack of attendance by physician-determined group B1. It should be noted that the charity hospital from which these data were collected experiences high no-show rates. This is due to a multitude of factors including transportation problems, lack of childcare support, and decreased social support to name a few. It could be that the HIV/AIDS population is at the higher end of the stressor continuum, which would decrease the likelihood for medical regimen adherence among a relatively non-adherent population. Thus, extra time for completion of the project or other methods for recruitment should have been considered.

Closing Remarks

In summary, while the current research did not support differences in groups based on health status using a median CD4 cell count split, with the exception of in the visual-spatial domain, this sample did show impairments that were generally Below Average/Mild, indicating some neuropsychological impairment in this HIV+ sample. So, while it appears that there is neuropsychological impairment that occurs during the progression of HIV/AIDS, it remains unclear when and/or under what circumstances this takes places. While the CD4 count in category B does not appear to be an adequate predictor, future research will have to examine whether health status can be useful for assessment and treatment purposes regarding neuropsychological impairment in individuals with HIV/AIDS.

No psychosocial predictors were found to be significant across all the domains, suggesting that outcomes for each of the tests may not be attributable to the same variable(s). While these findings may not have significant implications for neuropsychological impairment, it could be that each variable is only significant at specific stages in the HIV/AIDS progression, which requires further investigation. It could also be that the category B patients do not show significant neuropsychological impairment. This possibility applies to the comparison between groups within category B but also the category B group as a whole, which may also be evident in the other two categories (A and C). Future research should examine and compare all three categories, sampling from each of the nine cells and using multiple tests from each domain.   It is also recommended that future studies investigate longitudinal data to explore how individuals progress over time looking at health status and CD4 counts. This would allow for researchers to better understand how patients move within the health classification system over time, and possibly provide more information about the discrepancy in sample sizes within each of the cells in the health classification framework.

While this study may not have been successful in proving the health classification system as an effective model for identifying neuropsychological impairment based on health classification, hopefully it will guide future studies by highlighting potentially unexpected challenges and providing basic exploratory from which the field can build upon. Not only should the current model be evaluated to explore its utility in evaluating neuropsychological impairment but future studies may wish to seek out other possible models that may serve as useful tools for indicating the progression of neuropsychological impairment in patients with HIV/AIDS. Should an effective model be validated, researchers may wish to explore the

possibility of expanding this model to other health conditions where declines in

neuropsychological functioning are expected.

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Appendix A

Clinical Categories

CD4 (T-cell) Categories	A Asymptomatic or Acute HIV Infection	B Symptomatic (Not A or C)	C AIDS Indicator Condition
1. >500	A1	**B1**	C1
2. 200-499	A2	**B2**	C2
3. <200	A3	**B3**	C3

Health Planner: Clinical Categories (2001) EIC/EKLMC/LSUHSC

Consent to Participate in a Research Study

Subject #_____

Title of Study:
Neuropsychological Performance and Dementia Symptoms in HIV+ Predominantly African-American Population

Performance Sites:
We expect 60 participants to be gathered through the Early Intervention Clinic (EIC) and Earl K. Long Medical Center (EKLMC).

Investigators Involved in This Study:

Principle Investigator: Wm. Drew Gouvier, Ph.D.
                         (225) 578-4138
Co-Investigator: Kathleen E. Kendra, M.A.
                         (650) 493-5000 X63025

Purpose of the Study:
The purpose of this study is to explore the relationship between HIV health status and neuropsychological functioning.

Subjects:
To participate in this study, subjects must be diagnosed with HIV/AIDS and at least 18 years of age. Patients will be excluded from this study if they have been diagnosed with HIV/AIDS for less than 6 months. Patients will also be excluded if they have not had blood work completed in the past 9 months. Patients will be excluded if they are asymptomatic or have an AIDS indicator condition.

Study Procedures:
After obtaining informed consent, subjects' health status will be obtained by medical chart review. If patients are determined to be symptomatic, demographic information will be obtained. They will then be administered the brief neuropsychological battery. Measures will assess memory, language, attention and executive functioning, and symptom severity of depression and anxiety. Participation should take approximately 30-60 minutes.

Benefits of Participation in This Study:
No benefits are promised from your participation in this study. However, participation in this study should assist in the expansion of knowledge pertaining to the neuropsychological functioning of a subgroup of HIV+ individuals.

Risks to the Subject:
No known risks are identified as potential outcomes of your participation in this study. Graduate level students in clinical psychology, supervised by a licensed clinical neuropsychologist, will conduct this study. To ensure confidentiality, all testing materials will be kept safely in a locked cabinet in a research lab.

Right to Refuse:
Participation in this study is voluntary and subjects may change their mind and withdraw from the study at any time without penalty or loss of any benefit to which they may otherwise be entitled. Participants may contact Kathleen Kendra to withdraw from this study.

Subject's Right to Privacy:
This study is confidential. Participants will be assigned a research code. However, confidentiality is not absolute in that data will be kept confidential unless legally compelled.

Financial Information:
No monetary incentives will be offered for participation in this study. However, an edible incentive will be offered upon completion of the test battery.

Removal:
The participant will be removed from the study if, upon examination of demographic information inclusion criteria are not met, or if the individual does not complete the entire test battery.

Signatures:
This study has been discussed with me and all my questions have been answered. I may direct additional questions regarding study specifics to the investigators. If I have questions about subjects' rights or other concerns, I can contact Robert C. Mathews, Chairman, LSU Institutional Review Board, (225) 578-8692. I agree to participate in the study described above and acknowledge the researchers' obligation to provide me with a copy of this consent form if signed by me.

_____   _____
Subject Signature   Date

_____
Subject's Name Printed

Appendix C

Demographics

Subject Number:_____   EKL#:_____

Date of HIV/AIDS Diagnosis:_____   Date of Birth:_____

Sex: M   F   Age:_____

Marital Status: Singe   Married   Separated   Divorced   Widowed

Race: Caucasian   African American   Other:_____

Educational Level:_____

Employed: Yes   No

Collected from medical chart:

Most recent T-Cell (CD4 count): _____

Viral Load:_____

Clinical Category/HIV-severity: B1   B2   B3   Other:_____

Medications currently taking:

_____   _____

_____   _____

_____   _____

_____   _____

Vita

Kathleen E. Kendra received a Bachelor of Science degree in psychology at California Polytechnic State University- San Luis Obispo, in 2001, and a Master of Arts in psychology from Louisiana State University in 2004. She completed her internship requirements for a doctorate in psychology at Veterans Affairs Palo Alto Health Care System in 2007, and expects to receive the degree of Doctor of Philosophy from Louisiana State University in May 2008 under the guidance of Dr. Wm. Drew Gouvier. Ms. Kendra is currently working at the National Center for Posttraumatic Stress Disorder at Veterans Affairs Palo Alto Health Care System as a member of the screening and monitoring division of the Military Sexual Trauma Support Team.