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Pepperdine University

Graduate School of Education and Psychology

EXAMINATION OF THE ANTI-SACCADE TASK AS AN INDICATOR OF  
COGNITIVE FUNCTIONING IN HIV INFECTED INDIVIDUALS

A clinical dissertation submitted in partial satisfaction  
of the requirements for the degree of  
Doctor of Psychology

by

Katherine Clancy Olson

October, 2012

Cary Mitchell, Ph.D. – Dissertation Chairperson

This clinical dissertation, written by

Katherine Clancy Olson

under the guidance of a Faculty Committee and approved by its members, has been submitted to and accepted by the Graduate Faculty in partial fulfillment of the requirements for the degree of

DOCTOR OF PSYCHOLOGY

Doctoral Committee:

Cary Mitchell, Ph.D., Chairperson

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Curriculum Vitae  
Katherine Clancy Olson

EDUCATION

Doctor of Psychology in Clinical Psychology  
Pepperdine University, Graduate School of Education and Psychology (Los Angeles, CA)  
APA Accredited program  
Cumulative GPA 3.95  
Clinical Competence Exam passed June 2008  
Dissertation: Examination of the anti-saccade task as an indicator of cognitive functioning in HIV infected individuals, defended March 2012

Master of Arts in Psychology  
Pepperdine University, Graduate School of Education and Psychology (Los Angeles, CA)  
APA Accredited program  
Graduated with honors Summer 2006  
Cumulative GPA: 3.97

Bachelor of Arts in Psychology  
University of Southern Mississippi, Honors College (Hattiesburg, MS)  
Graduated Cum Laude December 1998  
Cumulative GPA: 3.45

CLINICAL TRAINING EXPERIENCE

APA-accredited Pre-doctoral Internship in Clinical Psychology  
Sharp Healthcare (Sharp Grossmont Hospital & Sharp Mesa Vista Hospital)  
San Diego, CA  
August 2009 – August 2010

- Facilitate and co-facilitate CBT-and DBT-based group therapy for Intensive Outpatient Programs, serving adults and older adults with severe mood/anxiety disorders, somatoform symptoms, Axis II diagnoses, thought disorders, and mild cognitive impairment
- Design and teach psychoeducational lectures on CBT and DBT concepts within inpatient units, outpatient programs, staff in-service meetings, and community events
- Receive psychodiagnostic and neuropsychological assessment referrals from diverse sources within the psychiatric hospital, including the medical psychiatric unit (serving patients with co-occurring psychiatric and significant acute medical illness), the specialized older adult unit, the locked psychiatric ICU, and open general adult units. Administer, score, and interpret test batteries, write reports, and provide feedback to referring physicians, patients, and caregivers as indicated
- Shadow and assist psychiatric liaison service in emergency department and on medical floors of 446-bed acute care hospital

- Consult and work cooperatively among a multidisciplinary team and, when indicated, provide case management, as well as individual, couples and family therapy sessions to support patients in inpatient and outpatient psychiatric care

#### Clinical/Research Neuropsychology Practicum

Cedars-Sinai Medical Center

Los Angeles, CA

September 2008 – August 2009

- Designed, administered, scored, and interpreted diagnostic assessments, cognitive screening batteries, and comprehensive psychological and neuropsychological evaluations
- Composed comprehensive test reports and conducted thorough feedback sessions with patients as appropriate
- Certified to administer test protocols for ongoing research on the synergistic effects of HIV infection and aging
- Provided focused treatment planning and appropriate follow-up care for adult patients with psychiatric diagnoses as well as with patients with medically based diagnoses such as brain tumors, chronic pain, spinal cord injuries, and other neurological disorders
- Received referrals from diverse sources including inpatient and outpatient neurorehabilitation, HIV clinical and research sources, pediatric and geriatric outpatient clinics, and psychiatric inpatient unit

#### Clinical Psychology Practicum

Ventura Youth Correctional Facility, California Department of Corrections

Camarillo, CA

August 2008 – June 2009

- Conducted brief and longer term individual psychotherapy as well as crisis interventions with adolescents and young adults utilizing primarily cognitive behavioral therapeutic techniques
- Co-facilitated a structured therapy group for young women based on dialectical behavior therapy concepts
- Worked with a population of correctional inmates primarily female, aged 16-24 and from diverse cultural, ethnic, and socioeconomic backgrounds

#### Neuropsychological Clerkship

LA County-USC Medical Center, Keck School of Medicine

Los Angeles, CA

August 2007 – August 2008

- Administered, scored, and interpreted more than two dozen multi-domain neuropsychological assessment batteries to patients at the Rand Schrader HIV Clinic
- Authored reports and made recommendations based on referral questions
- Consulted with referring psychiatrists and neurologists regarding patient care



- Conducted additional neuropsychological testing with patients enrolled in Frontotemporal Dementia Consortium study seeking to define a frontal variant of Alzheimer's Disease

#### Doctoral Practicum Externship

Union Rescue Mission - Pepperdine University Counseling Center

Los Angeles, CA

September 2006 – August 2008

- Conducted psychotherapy with a diverse population of men and women enrolled in a residential rehabilitation program and other needy individuals in the “skid row” area of downtown Los Angeles
- Duties included conducting comprehensive intake interviews, devising case conceptualizations, treatment planning, psychological assessments, report writing, seeking professional consultations, terminations, and presentation of case materials in supervision
- Common diagnoses among clientele included Substance Use/Abuse/Dependence, Unipolar and Bipolar Mood Disorders, Psychosis, PTSD, Anxiety Disorders and Personality Disorders

### ASSISTANTSHIP EXPERIENCE

#### Teaching Assistantship

Pepperdine University Graduate School of Education and Psychology

Los Angeles, CA

September 2007 – June 2009

- Provide support for yearlong doctoral-level Cognitive-Behavioral Theoretical Orientation course by preparing class materials and conducting research as requested by professor
- Assist professor with multiple units of Master's level course on Child and Adolescent Interventions, including preparing of materials, proctoring examinations, conducting research, and scoring examinations

#### Graduate Assistantship

Pepperdine University Graduate School of Education and Psychology

Los Angeles, CA

August 2005 – June 2009

- Provide administrative support to the University Director of Student Teaching
- Assist to guide graduate-level teaching credential candidates through the student teaching experience
- Work cooperatively with the University education department personnel to ensure that all students are eligible for student teaching as per California state guidelines

### ADDITIONAL WORK EXPERIENCE

#### Youth Counselor

Optimist Youth Homes and Family Services

Los Angeles, CA

November 2003 – August 2005 (full-time)

August 2005 – May 2006 (on-call, per diem)

- Maintained individual therapeutic caseload with residents in a Level-12 group home for at-risk youth from diverse ethnic and socioeconomic backgrounds
- Co-facilitated weekly family group therapy sessions and daily behavioral group therapy sessions
- Accompanied residents to Narcotics Anonymous meetings, anger management meetings, substance abuse counseling, medical/dental appointments and monthly psychiatric visits
- Created and executed enrichment and socialization programs

Internet Marketing Representative

Citysearch.com

Los Angeles, CA

November 2002 – November 2003

- Managed paid content for online city guides in markets of Nashville, San Antonio and New Orleans

Regional Sales Manager

Talent Tree, Inc.

Pasadena, CA

July 2002 – November 2002 (contracted interim position)

- Designed marketing plan, generated new business, and managed sales territory for Glendale, Burbank and Pasadena

Recruiter

Robert Half International, Inc.

Las Vegas, NV

January 1999 – July 2002

- Recruited, interviewed and placed candidates in job openings
- Developed and maintained working relationships with corporate clients
- Selected as Area Public Relations Spokesperson to act as a liaison between corporate PR department and local publications and broadcast stations

University Host

University of Southern Mississippi

Hattiesburg, MS

November 1997 – December 1998

- Selected as one of 25 from a nominated group of hundreds to represent University in recruiting, public, and government forums for a year-long internship

## PRESENTATIONS AND PUBLICATIONS

Hardy, D., Goodkin, K., Olson, K., Lopez, E., Morales, G. & Buitron, M. (2011)  
Antisaccade errors relate to working memory in older but not younger HIV-1 seropositive

adults. In: Abstracts of the Thirty-Ninth Annual Meeting of the International Neuropsychological Society in Boston, MA.

Olson, K. (2008) *An introduction to the humanistic theoretical orientation*. Invited guest lecture in Master's level curriculum course, hosted by Dr. David Elkins. Pepperdine University Graduate School of Education and Psychology, Los Angeles, CA.

Olson, K. (2008) *Case presentation from a Rogerian perspective*. Invited guest lecture at Workshop on Existential-Humanistic Psychology. Pepperdine University Graduate School of Education and Psychology, Los Angeles, CA.

Tarasewicz, J., & Clancy, K. (in review) *The Trouble with Tasha*. Children's book designed to help overweight and obese children develop coping skills to improve well-being.

Clancy, K., & Mackenzie, J. (2007) *Childhood obesity and mental illness*. In: Abstracts of the Annual Convention of the American Psychological Association in San Francisco, CA.

Mackenzie, J., Clancy, K., & Smolinski, S. (2006) *A student's perspective of getting through the University IRB process and applying to conferences*. Invited guest lecture at Master's level curriculum course, hosted by Dr. Jack Lipton. Pepperdine University Graduate School of Education and Psychology, Los Angeles, CA.

Smolinski, S., Clancy, K., & Mackenzie, J. (2006) *Cognitive dissonance: an exploration of academic cheating*. In: Abstracts of the Annual Convention of the American Psychological Association in New Orleans, LA.

Clancy, K., Mackenzie, J. & Smolinski, S. (2006) *An analysis of cognitive dissonance in academic cheating*. In: Abstracts of the Annual Conference of the Western Psychological Association in Palm Springs, CA.

### CONTINUING EDUCATION and TRAINING EXPERIENCE

Monthly Neuropsychology Research Committee at Cedars-Sinai Medical Center (2012, ongoing)

Ongoing seminars in psychodiagnostics, professional issues, and diversity issues hosted by Sharp Mesa Vista Hospital (2009 – 2010)

4<sup>th</sup> Annual HospiceCare Conference: A Guide to End-of-Life Care (November 2009, San Diego, CA)

Serving Older Women with Substance Use Problems, a workshop hosted by the American Society on Aging (November 2009, San Diego, CA)

7<sup>th</sup> Annual Conference of the American Academy of Clinical Neuropsychology (June 2009, San Diego, CA)

Weekly psychiatry grand rounds in Psychiatry and Behavioral Neurosciences hosted by Cedars-Sinai Medical Center (2008-2009)

20<sup>th</sup> Annual Los Angeles County Psychological Association Convention (October 2008, Culver City, CA)

HIV, Aging, and the Brain Seminar hosted by the City of West Hollywood and Cedars-Sinai Medical Center (September 2008)

Trauma-Focused Cognitive-Behavioral Therapy, a 10 CEU online training course hosted by the Medical University of South Carolina (September 2008)

18<sup>th</sup> Annual Nelson Butters' West Coast Neuropsychology Conference (April 2008, San Diego, CA)

Weekly psychological assessment didactic training series hosted by L.A. County – USC Medical Center Department of Psychiatry (2007 – 2008)

Humanistic/Existential Psychology Lab hosted by Dr. David Elkins, Pepperdine University (2007 - 2008)

115<sup>th</sup> Annual Convention of the American Psychological Association (August 2007, San Francisco, CA)

5<sup>th</sup> Annual Conference of the American Academy of Clinical Neuropsychology (June 2007, Denver, CO)

Monthly didactic training series on clinical psychology topics hosted by guest lecturers at the Union Rescue Mission (2006-2007)

Practical Pediatric Pain Management and End of Life Care Workshop hosted by Children's Hospital Los Angeles (October 2006)

114<sup>th</sup> Annual Convention of the American Psychological Association (August 2006, New Orleans, LA)

86<sup>th</sup> Annual Convention of the Western Psychological Association (April 2006, Palm Springs, CA)

## GRANTS AND FELLOWSHIPS

Pepperdine GSEP Colleagues' Grant (2005-2009)

Conrad H. Hilton Foundation Fellowship (2006-2007)

TEST ADMINISTRATION/INTERPRETATION CAPABILITIES

AD8 Dementia Screening  
Alzheimer's Quick Test  
American National Adult Reading Test Beck Anxiety Inventory  
Beck Depression Inventory II  
Beck Scale for Suicidal Ideation  
Beery Visual-Motor Integration  
Bender Gestalt  
Boston Naming Test  
California Verbal Learning Test II  
Category Fluency  
CLOX I & II  
Cognistat  
Cognitive Difficulties Scale  
Conner's Rating Scales  
Continuous Paired Associate Learning: Dual Task Paradigm  
Continuous Performance Test  
Controlled Oral Word Association Test  
Delis-Kaplan Executive Function System  
Dementia Rating Scale II  
Dot Counting Test  
Figural Visual Scanning & Discrimination  
Finger Tapping Test  
Folstein Mini Mental Status Exam  
Geriatric Anxiety Inventory  
Geriatric Depression Scale  
Grooved Pegboard  
Judgment of Line Orientation Test  
Kaufman Brief Intelligence Test  
McGill Pain Questionnaire  
Miller Forensic Assessment of Symptoms Test  
Millon Clinical Multi-Axial Inventory III  
Mini Mental Status Exam  
Minnesota Multiphasic Personality Inventory 2 & RF  
Montreal Cognitive Assessment  
N-Back  
Neuropsychological Assessment Battery  
Paced Auditory Serial Addition Test  
Personality Assessment Inventory  
Posner Letter Matching Test  
Pyramids & Palm Trees

Raven's Progressive Matrices  
 Repeatable Battery for the Assessment of Neuropsychological Status  
 Rey 15 Item  
 Rey Auditory Verbal Learning Test  
 Rey-Osterrieth Complex Figure  
 Rorschach (Exner scoring system)  
 Short Category Test  
 Sentence-Picture Verification Task  
 Simple & Choice Reaction Time (Go-No/Go Paradigm)  
 Stroop Task (Golden & Kaplan versions)  
 Structured Clinical Interview for DSM Disorders  
 Symptom Checklist 90  
 Test of Memory Malingering  
 Thematic Apperception Test  
 Trail Making Test A & B  
 Trauma Symptom Inventory  
 USC-REMT List Learning Task  
 Wechsler Abbreviated Scale of Intelligence  
 Wechsler Individual Achievement Test  
 Wechsler Memory Scale III  
 Wechsler Test of Adult Reading  
 Wechsler Adult Intelligence Scale III & IV  
 Wide Range Achievement Test IV  
 Wisconsin Card Sorting Test  
 Woodcock-Johnson Tests of Achievement III

### PROFESSIONAL ORGANIZATIONS and AFFILIATIONS

American Psychological Association

- *Division 40, Clinical Neuropsychology*
- *Division 12, Section II, Clinical Geropsychology*

Psychologists in Long Term Care

American Academy of Clinical Neuropsychology

National Association of Neuropsychology

Pepperdine University GSEP Student Government Association

- *First Year Student Representative*

Toastmasters International

Psi Chi Psychology Honor Society

Who's Who in American Colleges and Universities

National Dean's List

## Abstract

The advent of highly active antiretroviral therapy (HAART) regimens has resulted in significantly reduced morbidity and mortality due to HIV infection. However, in spite of more effective treatment options, for some individuals, HIV infection continues to be associated with clinically significant cognitive impairment, particularly in the later stages of disease. The purpose of the present study was to examine the usefulness of the anti-saccade task as a measure of cognitive impairment in a community sample of older HIV+ adults. Using an archival data set, this exploratory study examined how performance on the anti-saccade task related to the diagnosis of HIV-associated neurocognitive disorders. Specifically, the study focused on HIV-associated mild neurocognitive disorder (MND) and HIV-associated dementia (HAD). The presence of MND or HAD was diagnosed using participants' neuropsychological test performance and self-reported functional status. It was hypothesized that deficits in anti-saccade task performance would be associated with deficits on other measures of cognitive functioning and with diagnosis of HAD. There were 81 HIV+ adults in the sample. They had a mean age of 48.35 years and reported an average of just over 13 years of education. The HIV+ participants were predominantly male (69%) and African American (57%), with significant numbers of Caucasian (30%) and Hispanic (14%) persons as well. Overall, the HIV+ participants in this sample reported little functional impairment in their daily lives, performed relatively well on the neurocognitive measures, and showed little difficulty with the anti-saccade task. In general, the sample appeared relatively healthy, perhaps reflecting the improved treatments for HIV in recent years. The lack of variance on cognitive measures, including the anti-saccade task, made it difficult to test the study's hypotheses. Exploratory analyses showed modest but statistically significant correlations between anti-saccade



task performance and WAIS-R Digit Symbol scores. Considering both anti-saccade error rates and task scores, poorer performance was associated with lower scores on Digit Symbol. Other findings, limitations of the study, and suggestions for future research are discussed.

## Introduction

Clinical and scientific attention to cognitive and functional status among HIV-1 diagnosed individuals has grown significantly in recent years, as has the need for such findings. From 2004 through 2007, the estimated number of newly diagnosed HIV/AIDS cases in the 34 states of the U.S. with confidential name-based HIV infection reporting increased by 15% (CDC, 2007). HIV infection is the most common preventable and treatable cause of neurocognitive impairment in individuals under age 50 years (Ances & Ellis, 2007). HIV-1 is the form of the virus that causes disease in most of the world, including the United States, Europe, Asia, Latin America, and most of Africa, while HIV-2 is predominantly clustered in West Africa (CDC, 1998). Throughout this research, the term “HIV” refers to HIV-1 and this type of infection will be the sole focus of study.

The U.S. Centers for Disease Control and Prevention (CDC, 1992) assesses the clinical severity of HIV disease by the presence of specific HIV-related conditions. Clinical categories denoted by letters A, B, or C provide a classification system based on symptoms to identify disease stage. Clinical category “A” signifies asymptomatic conditions. Clinical Category “B” is defined by symptomatic conditions (a) attributed to HIV infection or (b) indicated by a defect in cell-mediated immunity and considered to have a clinical course or management that is complicated by HIV infection. Clinical Category “C” is identified by the presence of “AIDS-indicator” conditions, those that signal HIV infection that has progressed to a diagnosis of AIDS.

The American Psychiatric Association (Forstein et al., 2006) lists four central nervous system manifestations of direct HIV infection by disease stage, including (a) acute infection, (b) asymptomatic infection, (c) early symptomatic infection, and (d) late symptomatic infection. According to the APA (2000), prior to the introduction of highly

active antiretroviral therapy (HAART), in the asymptomatic stage there was a 20-30% prevalence of significant cognitive-motor impairment, while in early symptomatic infection, significant impairment occurred in up to 50% of patients. In late symptomatic infection (AIDS), impairment occurred in anywhere from 60 to 90% of patients. The advent of HAART regimens such as protease inhibitors, nucleoside analogue reverse transcriptase inhibitors and non-nucleoside reverse transcriptase inhibitors has resulted in decreased plasma viral load to levels as low as non-detectable, allowing for a significantly reduced morbidity and mortality due to HIV infection (APA, 2000). Moreover, since the introduction of HAART, research has shown a reduction in the prevalence of cognitive impairment among persons with HIV (APA, 2000), with levels of such impairment dropping to as low as 5% in the asymptomatic stage, 15% in early symptomatic infection, and 25% in late symptomatic infection among treated persons. Due to medical advances, namely HAART, many HIV+ individuals in industrialized countries now live upwards of 20 years after initial infection, even long after they have developed AIDS (World Health Organization, 2004). However, some studies suggest that neurocognitive impairment progresses despite use of HAART (Power, McArthur, & Johnson, 1994), and ultimately, the prevalence of clinically relevant impairment statistically increases with stage of disease. In summary, many new cases arise every day, and diagnosed patients are living longer, higher quality lives. However, in spite of effective treatment options, for some individuals, HIV infection continues to be associated with clinically significant cognitive impairment, which may in turn be associated with parallel declines in functional status.

The HIV Neurobehavioral Research Center (HNRC) at the University of California, San Diego (UCSD) (Cherner et al., 2007) has established three categories or levels of impairment for HIV-related neurocognitive complications including (a) Asymptomatic neurocognitive impairment (ANI), (b) HIV-associated mild neurocognitive disorder (MND), and (c) HIV-associated dementia (HAD). Collectively, these disorders are referred to as HIV-associated neurocognitive disorders, or HAND (Antinori et al., 2007). The two symptomatic diagnostic categories, MND and HAD, were the focus of the present research.

HNRC (2007) defines MND by multiple features including (a) acquired mild-to-moderate impairment in cognitive function documented by a score of at least one standard deviation below demographically-corrected norms on neuropsychological tests of at least two different cognitive domains; (b) cognitive impairment which interferes, at least mildly, with daily functioning; and (c) functional impairment that has been observed for  $\geq 1$  month. Additional exclusionary criteria require that (a) the impairment does not meet criteria for delirium or dementia, and (b) the impairment is not fully explained by comorbid conditions.

Diagnosis of HIV-associated dementia (HAD) according to HNRC's 2007 criteria requires: (a) acquired moderate-to-severe cognitive impairment documented by a score of at least 2 SD below demographically corrected normative means in at least two different cognitive areas, and (b) marked difficulty in activities of daily living due to the cognitive impairment. Additionally, the impairment should have been present for at least one month or more, not meet criteria for delirium or dementia, and not be adequately explained by comorbid conditions. Proper diagnosis of these conditions is extremely

important not only for treatment of the associated symptoms, but also in order to anticipate potential secondary effects of deficits such as lapses in medication compliance and appointment keeping.

The standards of the American Psychiatric Association's (2005) Office of HIV Psychiatry recommend the following components be included in a comprehensive evaluation of the HIV+ patient: (a) a general medical work-up; (b) a psychiatric work-up; (c) a cognitive screening work-up; and (d) a functional status assessment. Because both HAD and MND are diagnoses of exclusion, it is essential that any comprehensive evaluation rule out other etiologies of cognitive-motor impairment, and attention to rule-out diagnoses and etiologies for deficits should be of primary focus. Furthermore, since neuropsychiatric symptoms may improve with treatment and may wax and wane over time, serial monitoring is recommended.

One popular option for brief assessment, the Mini Mental Status Exam (MMSE) (Folstein, 1975; Pessin, Rosenfeld, Burton, & Breitbart, 2003) has been utilized despite the fact that it was originally validated for identifying Alzheimer's dementia and has many items that are representative of cortical functions. More recent research has demonstrated that neurocognitive decline is not readily detected by the MMSE unless the patient is severely demented (Skinner, Adewale, DeBlock, Gill, & Power, 2009). The MMSE may not be an ideal measure for the detection of cognitive deficits typically associated with HIV because many of the items on the evaluation map cortical dysfunction rather than subcortical cognitive changes. Since MND and HAD are both primarily subcortical processes, the MMSE may have limited sensitivity to identifying these disorders.

Several brief neuropsychological tests have been developed specifically for clinical use with an HIV+ population, including the HIV Dementia Scale (HDS) (Power, Selnes, Grim, & McArthur, 1995) and a derivative form, called the International HIV Dementia Scale (IHDS) (Sacktor, Wong, & Nakasujja, 2005); the Mental Alteration Test (Jones, Teng, Folstein, & Harrison, 1993); the Executive Interview (Berghuis, Uldall, & Lalonde, 1999); and the HIV Dementia Assessment (Grassi, Perin, Borella, & Mangoni, 1999). A popular measure in relatively wide use in clinical and research settings (Chang, Ernst, Leonido-Yee, & Speck, 2000; Chang et al., 1999), the HIV Dementia Scale (Power, Selnes, Grim, & McArthur, 1995) is comprised of four tasks: the anti-saccade task, a timed written alphabet measure, verbal word list memory recall, and written copy of a cube. The cutoff score for suspected HAD is ten (or less) of 16 in the sum total of all four tasks. The total score can also be pro-rated to exclude the anti-saccade task with a revised cut off score of less than 7.5 out of 12 (Davis, Skoloasky, Selnes, Burgess, & McArthur, 2002). While the HIV Dementia Scale is widely used, the anti-saccade task embedded within the measure deserves closer individual attention in part due to its limited reliance on language, which sets it apart from other brief screening measures. In particular, research is needed to determine the stand-alone clinical utility of the anti-saccade task in assessment of HIV infected individuals. Use of such a tool may be especially beneficial those who speak English as a second language who might otherwise be alienated by language-dependent measures.

In many patient populations, the anti-saccade task has emerged as an important measure for investigating the flexible control that an individual has over his or her behavior. It requires that participants must suppress the reflexive urge to look at a visual

target that appears suddenly in the peripheral visual field and must instead look away from the target in the opposite direction. In a typical anti-saccade task, the viewer fixates his or her gaze on a central location, a stimulus is flashed to one side of fixation, and the task is to not look at the location of the cue but rather to make an anti-saccadic eye movement in the opposite direction from where the cue was presented. If the viewer fails to refrain from responding to the cue, a pro-saccadic eye movement toward the cue will be generated before the anti-saccade (Guitton, Buchtel, & Douglas, 1985; Hallet, 1978; Hallet & Adams, 1980; Roberts, Hager, & Heron, 1994). A crucial step involved in performing this task is the top-down inhibition of this reflexive, automatic saccade. Success on this task, therefore, requires the ability to override the reflexive response of initiating a saccade toward a target and is tied to intact executive functions.

In the anti-saccade task, response suppression is required to resist moving the eyes toward the briefly exposed target. Whereas the superior colliculus mediates reflexive eye movements to visual targets, that is, pro-saccades (Hikosaka & Wurtz, 1985; Schiller, Sandell, & Maunsell, 1987), the frontal eye fields and dorsolateral prefrontal regions support the suppression of reflexive eye movement behavior, thereby enabling saccades in the opposite direction from the target, that is, anti-saccades (Guitton et al., 1985; O'Driscoll et al., 1995). Patients diagnosed with various neurological and/or psychiatric disorders that affect the frontal lobes or basal ganglia find it difficult to suppress the automatic pro-saccade, revealing a deficit in top-down inhibition (Munoz & Everling, 2004). Performance has also been shown to change with cognitive demands. For example, increasing working memory demands by adding an arithmetic task produces slower and less accurate performance (Roberts et al., 1994), suggesting a role of

executive functioning in this task. The neurocognitive areas utilized in the execution of this task make it a promising option as a screening measure for cognitive decline.

There are several populations for which the anti-saccade task has been demonstrated to be useful in examining cognition. Because of the dependency on frontal and basal ganglia structures, the anti-saccade task has emerged as an important clinical tool for investigating development and dysfunction in various neurological and psychiatric disorders (Leigh & Kennard, 2003; Everling & Fischer, 1998). Many patient groups have been studied using the anti-saccade task and key findings have been interpreted in the context of established neurophysiological findings to make specific predictions about how pathophysiology can influence top-down inhibitory control of saccade neurons and accumulation of activity toward the saccadic threshold (Munoz & Everling, 2004). A number of studies have shown that patients with schizophrenia perform poorly on anti-saccade tasks, with two common findings being increased error rates and prolonged reaction times for correct anti-saccades (Broerse, Crawford, & den Boer, 2001). Both adults and children diagnosed with ADHD have distinct difficulties in suppressing the automatic pro-saccade on anti-saccade trials (Munoz, Armstrong, Hampton, & Moore, 2003). Interestingly, among this population, there is no change in the mean reaction time of correct anti-saccades despite the increase in direction errors, implying that there is no deficit in the ability to initiate a voluntary response. Reaction times for correct anti-saccades are significantly increased in patients with Parkinson's Disease (Chen, Chen, & Tsai, 1999; Briand, Strallow, Hening, Poizner, & Sereno, 1999) indicating that the activity required to trigger correct anti-saccades might accumulate more slowly in these patients. This effect is not surprising since one of the hallmarks of



Parkinson's disease is a decreased ability to generate voluntary responses (Lezak, 2005). While the research findings and clinical implications for these populations may be dissimilar from those of the cognitively impaired HIV+ individual, consideration of previous research findings demonstrates that the anti-saccade task may be a suitable test of inhibitory control and the ability to generate voluntary actions. It therefore appears promising as an avenue for further study with alternate populations, including HIV+ individuals.

Two research questions were examined as part of the current study. First, how do HIV+ individuals perform on the anti-saccade task? Second, how does performance on the anti-saccade task relate to cognitive impairment and diagnoses of MND and HAD among HIV+ men and women? This study provided an opportunity to explore the sensitivity and specificity of the anti-saccade task as a measure of MND and HAD among HIV+ individuals. It was hypothesized that severe deficits in anti-saccade task performance would be associated with performance deficits on other measures of cognitive functioning. It was also hypothesized that deficits in anti-saccade performance would be associated with diagnosis of HAD among HIV+ individuals.

If significant associations were found between anti-saccade task performance and related diagnoses of cognitive impairment, then routine implementation of the anti-saccade task as a screener for cognitive complications in HIV+ individuals could be a time- and cost-effective strategy for the identification of potential neuropsychological decline in a primary care environment. Because the anti-saccade task is a less-language dependent measure than many screening measures commonly used (e.g., memory recall exercises, spontaneous list generation, or self-report measures), it may show promise for

clinics in communities where English is commonly a second language among patients seeking care. This could provide health professionals with a useful indicator of when a referral for further neuropsychological screening and assessment might be appropriate. Benefits of proper screening by the medical community potentially include (a) identifying patients who may benefit from further neuropsychological testing and/or neurological referral, (b) identifying deficiencies that might influence treatment compliance, and (c) improving accuracy in the prediction of prognosis.

## **Method**

### **Research Context and Design**

The data set used in this study was derived from a longitudinal study that attempted to determine the extent to which aging affects the presentation of progression of HIV-1 infection in terms of neuropsychological (NP) test performance and impairment, HIV-1-associated cognitive-motor disorders, functional status in activities of daily living, immunologic measures, and virologic measures. The original study was proposed as a two by two design comprised by (a) age category with two levels: younger (ages 18 to 39) and older (age  $\geq 50$ ); and (b) HIV serostatus with two levels: HIV+ and HIV-. The research was initially conducted at the University of Miami in Miami, FL with Karl Goodkin, M.D., Ph.D. as principal investigator, and later continued at Cedars-Sinai Medical Center in Los Angeles, California. Permission to utilize the archival data set was granted in writing from Dr. Goodkin and from Enrique Lopez, Psy.D., Senior Clinical Research Neuropsychologist at Cedars-Sinai. The present study utilized participant data collected both at the University of Miami and at Cedars-Sinai Medical Center. Data used in the present research was collected between December 1999 and August 2009. Participants were compensated \$200 for their first year of participation in

the parent study (all derived data for current research was sourced from first year visits), with the potential for a total of \$630 in total compensation over the course of three years.

The present study included both exploratory and correlational research design elements. The overall purpose was to explore the extent to which performance on the anti-saccade task was associated with relevant diagnoses of cognitive decline among HIV+ individuals. In addition, the researcher examined the extent to which determination of cognitive impairment by means of the anti-saccade task alone corresponded to the determination of cognitive impairment by more traditional means (i.e., through the use of multiple neuropsychological measures and functional assessment data). Because this was an archival study, the researcher did not have the ability to modify the research procedures or collect additional data.

### **Procedure**

In the current research study, a three-step process was planned to determine if performance on the anti-saccade task was in fact associated with cognitive decline in HIV-infected individuals. Initially, participants from the original study who met criteria for assignment to the MND or HAD groups were identified, based on their performance on neuropsychological and functional measures. Next, study participants were assigned to MND or HAD groups solely on the basis of the number of errors on the anti-saccade task (i.e., independent of performance on other neuropsychological or functional measures). Finally, to determine the predictive value of the anti-saccade task, the concordance between these two methods for assigning HIV+ individuals to MND and HAD groups was examined. The researcher obtained approval from Pepperdine University's Graduate and Professional Schools Institutional Review Board prior to beginning any work with the archival data set. As will be described in greater depth and

presented with results and discussion of data, the initial step of assigning participants to the MND or HAD groups proved problematic due to the relatively low numbers of persons with severe impairment and the lack of concordance between neuropsychological and functional measures. Therefore, it was necessary to adjust how the initial classifications were made, in order to respond to challenges encountered with the archival data set.

### **Participants**

Through August 2009, a total of 279 participants had completed assessments, met inclusionary/exclusionary criteria, and been entered into the parent study database. Of these, a total of 119 patient records had recorded anti-saccade task scores and error rates necessary for inclusion in the present study. A further review of completeness of neuropsychological and functional status data was also necessary with the potential for participants to be eliminated based on absence of critical data, and an additional five participants were eliminated based on missing critical data in their neuropsychological testing batteries. A final number of 114 participants possessed sufficient data in anti-saccade, functional, and neuropsychological measures to be included in the final analysis. For patient records in which data was available for both baseline assessment and subsequent annual follow-up assessments, only the first visit in which the required elements of data were collected (i.e., anti-saccade task scores and cognitive/functional measure scores to designate diagnostic category) was included in the present study. Of the 114 participants that had sufficient data to be included in the final analysis, 18 were missing one or more scores from their neuropsychological assessment battery, but had a sufficient amount of data to calculate functioning within all representative domains. In these 18 cases, their HAND-related diagnoses could still be calculated according to

procedures described previously despite these missing scores. The demographic characteristics of the participants in the present study are summarized, described, and presented with the research results.

Inclusion criteria approved for men and women participating in the original study were as follows: (a) for those HIV+ individuals, early or late symptomatic clinical disease stage; (b) membership in one of two age groups- 18-39 or  $\geq 50$  years of age; (c) willingness to provide documentation of HIV serostatus (HIV+ or HIV-) or be tested if serostatus was unknown; (d) willingness to participate for five years; and (e) English as the primary language of predominant usage. Exclusion criteria for the original cohort were: (a) current, systemic, acute opportunistic infection or tumor requiring chemotherapy; (b) current CNS infections or tumors associated with HIV infection that would potentially interfere with neuropsychological testing or completion of the study procedures; (c) severe HAD, by AAN 1991 criteria (exclusion necessary to ensure ability to perform the neuropsychological test battery); (d) non-HIV associated neurological disease (e.g., history of epilepsy, non-correctable visual or hearing impairments, prior cerebrovascular accident, Alzheimer's disease at entry, or multi-infarct dementia); (e) history of or current major psychiatric disorder (e.g., schizophrenia, bipolar affective disorder, or major depressive disorder); (f) mental retardation, learning disorders, motor skills disorder, disruptive behavior and attention deficit disorders, and pervasive developmental disorder; (g) current alcohol or substance dependence or history of alcohol or substance abuse disorder within the past three months; (h) collagen vascular disease; (i) severe chronic obstructive pulmonary disease (i.e., resting hypercarbia, O<sub>2</sub> or steroid dependency); (j) severe congestive heart failure (class IV); (k) unstable angina; (l)

myocardial infarction within prior 6 months; (m) use of systemic steroids (catabolic or anabolic); (n) hepatic failure; (o) renal failure; (p) immunostimulant therapies and other trials of non-FDA-approved ARV medications; and (q) residence outside of counties within and adjacent to the data collection sites.

At the evaluation appointment of the parent study from which the present research was derived, information was provided to the potential subjects on the goals of the research, the time commitment (number of evaluations and time per evaluation), and the study procedures (cognitive tasks, psychosocial instruments, psychiatric interview and rating, history and physical examinations, blood samples, and urine toxicology screens). Opportunity was given to respond to any questions. Staff then obtained the signed informed consent forms, written permission for HIV antibody testing, a bilateral medical release form with the primary care provider, and required HIPAA forms. Each participant in the study submitted to a medical history and physical examination, review of existing medical records on bilateral release, collection of cognitive data via neuropsychological testing, collection of clinical laboratory measures of HIV progression for immunologic and virologic research purposes, ratings of functional status, and specimen submission to a plasma and peripheral blood mononuclear cell repository.

### **Instruments**

**Anti-saccade task.** The anti-saccade task that was used in this research is a task embedded within the widely recognized HIV Dementia Scale, developed by Power, et al., (1995). The HIV Dementia Scale (HDS) consists of four tasks including a timed written alphabet measure, the anti-saccade task, a verbal word list memory recall, and written copy of a cube. The time taken to complete the written alphabet is converted to a

numerical score, with a maximum score of six. The total number of errors in 20 trials of the anti-saccade task is converted into a maximum score of four. Recall performance is measured with one point given for each word recalled spontaneously or one-half point for each word recalled with a semantic clue, for a maximum score of four. Time taken to copy the cube is converted to a maximum numerical score of two. The cutoff score for suspected HAD is ten (or less) of 16 in the sum total of all four tasks. The HDS rates well in both reliability and validity; it has demonstrated a sensitivity of 80%, specificity of 91%, and positive predictive value of 78% (Power et al., 1995).

As described previously, the anti-saccade task is a brief neurological measure designed to ascertain the level of control that an individual has over his or her behavior. It requires that participants must suppress the reflexive urge to look at a visual target that appears suddenly in the peripheral visual field and must instead look away from the target in the opposite direction. In a typical anti-saccade task, the viewer fixates his or her gaze on a central location, a stimulus is flashed to one side of fixation, and the task is to not look at the location of the cue but rather to make an anti-saccadic eye movement in the opposite direction from where the cue was presented. Trials may be administered by machine or manually by hand, as they were in this study. Directions for standardized administration of the anti-saccade task were as follows:

Hold both hands up at patient's shoulder width and eye height, and ask patient to look at your nose. Move the index finger of one hand, and instruct patient to look at the finger that moves, then look back to your nose. Practice until patient is familiar with task. Then, instruct patient to look at the finger that is NOT moving. Practice until patient understands task. Perform 20 trials. (Power et al., 1995)

An error is recorded when the patient looks towards the finger that is moving. The number of errors in 20 trials determines the total score, where less than or equal to three errors equals a score of four; four errors equals a score of three; five errors equals a score of two; six errors equals a score of one; and more than six errors equals a score of zero. To summarize and clarify, lower scores on the task are associated with more errors and therefore greater impairment. In the parent study, the task was administered by medical residents during the participants' medical evaluation appointment. Results were recorded manually as part of the HIV Dementia Scale (Power et al., 1995) in the parent study. However, the anti-saccade results were not previously examined or considered as an independent score. For the present study, two anti-saccade scores were recorded and examined: the task score as described above and the raw number of errors.

**Neuropsychological measures.** Seven domains of neuropsychological functioning were examined as part of the larger study from which the present archival data set was obtained, as recommended by the guidelines established by the NIH for the assessment of an HIV+ population. The domains were attention, speed of information processing, episodic memory, executive functioning/abstraction, language skills, visuospatial skills, and motor functioning. Within each of these domains, certain measures were selected by the researcher (under advisement of a co-researcher on the parent study) as representative of performance in that domain. The two measures selected to represent attentional capabilities were the Variable Interval Reaction Time (VIT) Test and WAIS-R Digit Span. The VIT Test is a simple visual reaction time task in which the interval between the warning signal and the imperative signal (a color block) varies among 25, 250, 500, 750, and 1000 milliseconds (Wilkie et al., 2004). The Digit



Span subtest of the WAIS-R requires individuals to repeat a chain of verbally presented numbers initially forwards, then backwards (Wechsler, 1981).

For speed of information processing, three measures were considered: the average decision time of the Go-No Go Paradigm, the Posner Letter Matching task, and the Figural Visual Scanning and Discrimination test. The Go-No Go Paradigm is a computer-based task with three conditions: (a) simple reaction time requiring recognition of a red block on the screen, (b) simple reaction time requiring recognition of a blue block on the screen, and (c) a reversal condition in which the individual is to ignore the red and respond only to the blue signal (Wilkie et al., 2004). The Posner Letter Matching task is used to measure the speed of accessing overlearned information (letters of the alphabet) from long-term memory by presented paired letters in a computer-based task to assess central processing speed relatively independent of motor speed (Wilkie et al., 2004). The Figural Visual Scanning and Discrimination test (Elkstrom, French, Harman, & Dermen, 1987) is a timed, 20 trial paper-and-pencil task requiring the participant to scan and discriminate between four figures to determine which is a match for the prototype with total time elapsed being the variable of interest.

Two measures were selected to represent episodic memory: the California Verbal Learning Test (total score and free delay recall) and WMS-R Logical Memory delayed score. The California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987) is a list learning exercise with multiple cued and free recall tasks at both immediate and delayed time frames designed to assess verbal memory. The Logical Memory subtest of the WMS-R (Wechsler, 1981) queries individuals on immediate and 30-minute delayed recall of short stories.

For executive functioning/abstraction, timed performance of Trail Making Test Part B, Wisconsin Card Sorting Test perseverative errors, and interference score on the Stroop Task were utilized. Part B of the Trail Making Test consists of 25 circles distributed over a sheet of paper including numbers 1 – 13 and letters A – L (Lezak, Howieson, & Loring, 2004). The patient draws lines to connect the circles in an ascending pattern, alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.) as quickly as possible without lifting the pen or pencil from the paper. The Wisconsin Card Sorting Test consists of four key cards and 128 response cards with geometric figures that vary according to three perceptual dimensions (color, form, or number). The task requires individuals to determine the correct classification principle using trial and error and examiner feedback (Heaton, Chelune, Talley, Kay & Curtis, 1993). The Stroop Color and Word Test consists of a word page with color words printed in black ink, a color page with 'Xs' printed in color, and a color-word page with words from the first page printed in colors from the second page (Golden & Freshwater, 2002). The respondent reads words or names the ink colors as instructed as quickly as possible within a time limit, providing three scores based on the number of items completed on each of the three stimulus sheets.

To assess language skills, the Boston Naming Test total score was used as well as the total scores on both the Controlled Oral Word Association Test and Category Fluency Task. The Boston Naming Test is a 60-item confrontation naming test of pictures ordered from easiest to most difficult that measures word retrieval performance (Strauss, Sherman, & Spreen, 2006). The Controlled Oral Word Association Test is a timed phonetic spontaneous list generating exercise in which individuals name common

everyday words beginning with the letters F, A, and S (Ruff, Light, Parker, & Levin, 1996). The Category Fluency Task (Spreen & Strauss, 1998) is a timed semantic list generating exercise in which individuals name as many animals as they can spontaneously.

Visuospatial skills were measured by timed performance on WAIS-R Digit Symbol and total score on WAIS-R Block Design. The Digit Symbol subtest of the WAIS-R (Wechsler, 1981) requires that the test taker writes down the corresponding symbol for a chart of numbers according to a provided key of digit-symbol pairs as fast as possible. The Block Design subtest of the WAIS-R (Wechsler, 1981) is a timed task that requires an individual to use blocks marked with white sides, red sides, and red/white sides to copy a specified pattern demonstrated by a prototype.

Finally, for motor functioning, timed performance on two measures was utilized: the WAIS-R Digit Symbol subtest and non-dominant hand performance on the Grooved Pegboard. As described above, the Digit Symbol subtest of the WAIS-R (Wechsler, 1981) requires that the test taker writes down the corresponding symbol for a chart of numbers according to a provided key of digit-symbol pairs as fast as possible. The Grooved Pegboard task is a manipulative dexterity assessment that tests fine motor skills in a timed manner. (Strauss et al., 2006).

Levels of cognitive impairment were assessed by determining if the participant's performance on these neuropsychological measures was more than one or two standard deviations below the mean scores in each of the seven domains. Criteria for impairment were consistent with Antinori et al. (2007), which defines impairment in neuropsychological testing performance in MND by a score of at least one standard

deviation below demographically-corrected norms on neuropsychological tests in at least two different cognitive domains, and in HAD by a score of at least two standard deviations below demographically corrected normative means in at least two different cognitive domains. Demographically-corrected normative data for neuropsychological tests were primarily sourced from scoring manuals and peer-reviewed published research. When such resources were not applicable or available, internal norms derived from the scores of the youngest (i.e. aged 18-39) HIV- participants were utilized. All scoring of neuropsychological measures had been completed by the principal investigators of the parent study, with z-scores made available for reference in the current research.

Because the number of tests varied within domains, a process for determining impairment within domains was established as follows: For domains in which there were two tests represented (i.e., attention, visuospatial skills, and motor functioning), both test scores had to be the requisite number of standard deviations below the mean as identified by Antinori et al. (2007) in order for one of the two impairment levels to be assigned. For domains in which there were three tests represented (i.e., speed of information processing, executive functioning/abstraction, and language skills), at least two of the three test scores had to be the requisite number of standard deviations below the mean. For episodic memory, the only domain in which there were four tests represented, at least three of the four test scores had to be the requisite number of standard deviations below the mean in order for an impairment category to be assigned.

**Functional measures.** The degree of functional impairment was ascertained by self-report of perceived cognitive dysfunction as defined by the Cognitive Difficulties Scale (CDS; McNair & Kahn, 1983), Patient Version. This measure requires that

respondents rate on a Likert scale how often, from 0 (not at all) to 4 (very often), they believe that they have experienced difficulty on various tasks related to attention, concentration, orientation, memory, praxis, language, and general daily functioning within the past month. The CDS has demonstrated high correlation with performance on neuropsychological measures of memory and attention ( $r = 0.51$ ) and good test-retest reliability ( $r = 0.77$ ) (Spitznagel, Tremont, Brown, & Gunstad, 2006). This assessment tool is consistent with Antinori et al.'s (2007) criteria for functional impairment, which defines MND as characterized by impairment that interferes at least mildly with daily functioning and has been observed for at least one month. HAD is characterized by marked difficulty in activities of daily living due to the cognitive dysfunction, and such impairment must be observed for at least one month.

### **Analyses**

Descriptive statistics were calculated on all of the measures utilized in this study, as well as on the participant demographic variables. Correlations between the anti-saccade error rates, task scores, and other cognitive measures were calculated. In order to determine if the anti-saccade task may be useful in predicting the level of cognitive impairment in HIV-infected individuals, the original research plan was for study participants to first be categorized into either MND or HAD diagnostic categories. While originally it was proposed to use both neuropsychological and functional measures collectively to determine these categorizations, it was later determined that only neuropsychological scores would be used due to multiple complications with the data, most notably including discordant findings of impairment between the functional and neuropsychological measures. Factors in and specifics of the decision to change criteria for diagnoses are presented in thorough detail with results and discussion of findings.

The two categories of impairment were to be formed a second time using only the performance scores (both raw errors and scaled scores) on the anti-saccade task. Categorized groups would then be compared using a two-by-two contingency table. If the diagnosis (either MND or HAD) as determined by neuropsychological/functional measures was consistent with the diagnosis as determined by the anti-saccade task, it would be recognized as a positive finding. Conversely, if the diagnosis (either MND or HAD) as determined by neuropsychological/functional measures was inconsistent with the diagnosis as determined by the anti-saccade task, it was recognized as a negative finding. Evaluation of the total numbers of positive and negative findings determined the usefulness of the anti-saccade task as a predictor of cognitive decline in HIV-infected individuals.

Use of the receiver operating characteristic (ROC) curve, whereby true positive rates and false positive rates are used to create a mapped statistical curve, was employed. ROC graphs are a useful technique for organizing classifiers and visualizing their performance, and are commonly used in medical decision making (Fawcett, 2004). Because ROC graphs are based upon the true positive and false positive rates in which each dimension is a strict columnar ratio (Fawcett, 2004), it does not depend on class distribution, making it especially useful for this archival study in which data can no longer be collected.

The sensitivity of any diagnostic test is the proportion of patients for whom the outcome is positive (i.e., who actually have the disorder or condition) that are correctly identified by the test, while the specificity is the proportion of patients for whom the outcome is negative (i.e., those who do not have the disorder or condition) that are

correctly not identified by the test (Bewick, Cheek, & Ball, 2004). The true positive rate is equivalent to sensitivity and the false positive rate is equal to  $1 - \text{specificity}$ , making the two-by-two contingency and ROC curve relevant tools in this statistical analysis. In the case of this research, the plan was for both the sensitivity and specificity of the anti-saccade task to be examined in order to assess its usefulness for the diagnosis of cognitive impairment by comparing it to established methods for determining cognitive impairment among HIV+ individuals. Positive predictive value (PPV) is defined by the probability that there will be a positive outcome whereas the negative predictive value (NPV) is the probability that there will be a negative outcome (Bewick et al., 2004). In the present study, a positive outcome was defined as a consistent diagnosis (i.e., both the neuropsychological/functional measures and the anti-saccade task would identify the same individuals in the same diagnostic category), and a negative outcome was defined as an inconsistent diagnosis.

## **Results**

### **Changes to Methods**

After the researcher performed the initial analyses for the present study, several changes to the research plan had to be made due to characteristics of the data. Two neuropsychological tests in the Speed of Information Processing domain had to be excluded from the analyses for determining MND and HAD diagnosis: the Posner Letter Matching Task and the Go-No Go Paradigm. After reviewing the data for the current study, it was determined that there was insufficient data present to provide a reliable standardized score for participants in the records for either of these tests. To make up for the loss of this data, the scaled score from the WAIS-R Digit Symbol subtest was utilized

as a substitution. This still allowed for two measures in the domain, which was sufficient to determine impairment via commonly applied standards (Antinori et al., 2007). So as to not utilize Digit Symbol in three different domains, Grooved Pegboard, non-dominant hand, was the only test used to measure motor skills.

One additional test was added to the domain of Episodic Memory, the delayed free recall score from the WMS-R Logical Memory subtest, when it was determined that sufficient data was present for analysis. This allowed for a more robust measurement of the domain. The Logical Memory subtest (Wechsler, 1981) requires the oral presentation of a narrative story to the examinee for immediate and delayed recall.

Initially, it was planned to establish diagnosis (MND, HAD, or No Diagnosis) by utilizing the z-scores for participant performance on both neuropsychological and functional measures. However, there was a major discrepancy between findings on neuropsychological measures and the self-report Cognitive Difficulties Scale (CDS) used to determine functional status. The majority of HIV+ participants diagnosed with MND or HAD according to results of neuropsychological testing did not show commensurate levels of self-reported functional impairment on the CDS. Had the original research plan been followed, the number of participants classified with MND or HAD on the basis of both neuropsychological and functional measures would have been so few as to make any additional analyses impossible. Therefore it was deemed necessary to revise the criteria for initial diagnosis to include only neuropsychological test performance; precise details of this amended procedure are presented with results and discussion.



## Demographic Characteristics of Participants

Descriptive statistics were calculated for all 114 participants and are presented in Table 1. Participants had an average of 12.94 years of education ( $SD = 2.54$ ), with 73 (64%) being male and 41 (36%) being female. Average age was 47.03 ( $SD = 12.27$ ), although it bears repeating that the age range of participants was restricted to 18-39 and 50+ in the parent study, such that all persons aged 40-49 were excluded. Ethnicities of participants were divided into three categories, with 61 who identified themselves as African American (53%), 17 as Hispanic (14%) and 36 as Caucasian (32%). No other ethnic identities were reported. Regarding handedness among participants, 106 (93%) were right-handed and 8 (7%) were left-handed.

Among HIV+ participants ( $n = 81$ ), there was an average of 13.01 years of education ( $SD = 2.59$ ), with 56 (69%) being male and 25 (31%) being female. Average age was 48.35 ( $SD = 11.68$ ). Ethnicities of HIV+ participants were divided into 46 who identified themselves as African American (57%), 11 as Hispanic (13%) and 24 as Caucasian (30%). Regarding handedness among HIV+ participants, 76 (94%) were right-handed and 5 (6%) were left-handed.

Among HIV- participants ( $n = 33$ ), there was an average of 12.79 years of education ( $SD = 2.46$ ), with 17 (52%) being male and 16 (48%) being female. Average age was 43.76 ( $SD = 13.21$ ). Ethnicities of HIV- participants were divided into 15 who identified themselves as African American (45%), 6 as Hispanic (18%) and 12 as Caucasian (36%). Regarding handedness among HIV+ participants, 30 (91%) were right-handed and 3 (9%) were left-handed.

### **Diagnostic Findings Utilizing Neuropsychological and Functional Measures**

Diagnoses of MND and HAD were to be determined by inclusion of results from both neuropsychological and functional measures. Among the 81 HIV+ participants, there were 29 assigned to the MND diagnostic category by scoring at least one (but less than two) standard deviations below the mean in two or more neuropsychological domains. The CDS, i.e., the self-report measure of functional impairment, assigned just four participants to the MND diagnostic category by a score of at least one (but less than two) standard deviations below the mean score on the measure. If, as originally planned, participants had been diagnosed with MND according to a combination of neuropsychological and functional measures, only two participants would have met diagnostic criteria for MND on both measures. Three participants were assigned a HAD diagnosis based on neuropsychological test performance (scores two or more standard deviations below the mean in two or more domains), while six were identified as HAD based on CDS score (two or more standard deviations beyond the mean score on the measure). Of these, only one participant would have met diagnostic criteria for HAD on both measures. Therefore, in order to provide some potentially useful analyses with the present data, it was decided by the researcher, with advisement from the co-principal investigator of the parent study, to classify patients with MND or HAD using neuropsychological measures only. Using this revised criteria, a total of 29 participants were assigned a diagnosis of MND and three participants were assigned a diagnosis of HAD. Collectively, 32 of the 81 HIV+ participants (39.5%) were assigned with some degree of HIV-associated neurocognitive disorders (HAND).

### **Anti-Saccade Task Performance**

In order to address the first research question regarding how HIV+ individuals perform on the anti-saccade task, error rates and task scores were calculated and are presented in Tables 2 and 3. Among the 81 HIV+ participants, 41 participants produced zero errors on the anti-saccade task; six participants produced one error; 18 participants produced two errors; eight participants produced three errors, five participants produced four errors, two participants produced five errors, and one participant produced six errors. No participants produced greater than six errors on the task. When using these error rates to calculate anti-saccade task scores according to the instructions on the HIV Dementia Scale, 73 participants (90%) received a score of four, the maximum score possible on the task; five participants received a score of three; two participants received a score of two; and one participant received a score of one. Overall, HIV+ participants demonstrated very good performance on the anti-saccade task, with fewer errors than might have been expected, and as a result, higher task scores.

Among the 29 HIV+ participants who were assigned a diagnosis of MND according to their performance on neuropsychological measures, 14 participants produced no errors; three participants produced one error; five participants produced two errors, three participants produced three errors, one participant produced four errors, two participants produced five errors, and one participant produced six errors. When using these error rates to calculate an anti-saccade task score according to the instructions on the HIV Dementia Scale, 25 participants (86%) received a maximum score of four; one participant (3.45%) received a score of three; two participants (7%) received a score of two; and one participant (3.45%) received a score of one. As these scores indicate, the

vast majority of HIV+ participants diagnosed with MND performed quite well on the anti-saccade task.

Among the three HIV+ participants who were assigned a diagnosis of HAD according to their performance on neuropsychological measures, one participant produced zero errors and two participants produced four errors. When using these error rates to calculate an anti-saccade task score according to the instructions on the HIV Dementia Scale, one participant (33.34%) received a maximum score of four and two of these participants (66.67%) received a score of three.

When comparing anti-saccade task performance among HIV+ participants and those diagnosed with MND or HAD, care must be taken in interpretations due to the discrepancy in sample size. However, with that in mind, it is interesting to note that the mean number of errors among HAD diagnosed participants ( $2.67, n = 3$ ) was greater than that obtained by MND diagnosed participants ( $1.45, n = 29$ ), or than that obtained by the entire sample of HIV+ participants ( $1.26, n = 81$ ). When these error figures are used to calculate task scores, the differences were less distinct among HAD diagnosed participants, MND diagnosed participants, and total HIV+ participants with mean scores of  $3.34 (SD = 0.58)$ ,  $3.72 (SD = 0.75)$ , and  $3.85 (SD = 0.50)$ , respectively. Once again, the relatively high average task scores reflected good anti-saccade performance across groups.

### **Association between Anti-saccade Task Performance and Diagnoses of MND and HAD**

A second research question sought to determine how performance on the anti-saccade task related to cognitive impairment and diagnoses of MND and HAD among HIV+ men

and women. Given that 26 of 32 (81%) HIV+ persons with diagnoses of MND or HAD obtained maximum scores of 4 on the anti-saccade task, overall it appeared that a HAND diagnosis was not associated with impaired performance on the anti-saccade task for most of these HIV+ participants. It was hypothesized that deficits in anti-saccade performance would be associated with a diagnosis of HAD among HIV+ individuals. However, since only three HIV+ participants were diagnosed with HAD, and of these, none demonstrated a large number of errors on the anti-saccade task, there were insurmountable challenges in attempting to test this hypothesis. Nevertheless, to further assess the relationship between anti-saccade task performance and diagnoses of MND and HAD among HIV+ participants, sensitivity and specificity values were calculated between performance on the anti-saccade task (error rate and task score) and diagnosis via neuropsychological measures. While the findings related to sensitivity and specificity are reported in full below, it is worth noting in advance that the small number of participants achieving anti-saccade scores suggestive of impairment, along with an uneven distribution of scores, made rendered these analyses both insignificant and of questionable value. As a result, the planned two-by-two contingency table, whereby HAND diagnoses based on neuropsychological test performance and functional status self report would have been compared with HAND diagnoses based on anti-saccade task performance, could not be executed due to the absence of useful cutoff scores that would have been provided by usable sensitivity and specificity findings. Regardless, the data related to sensitivity and specificity is reported below.

**Sensitivity of Anti-saccade Task.** The sensitivity of the anti-saccade task represents the proportion of HIV+ participants who have been classified as having MND

and HAD due to impaired performance on neuropsychological measures that are also identified as having MND and HAD due to impaired performance on the anti-saccade task. This would be considered a positive outcome, in that the findings would be congruent. In order to assess the sensitivity of the anti-saccade task, diagnoses of MND and HAD (both independently and collectively) were compared with error rates and task scores on the anti-saccade task. As stated previously, the small number of participants achieving anti-saccade scores suggestive of impairment and uneven distribution of scores made these analyses largely insignificant. Nonetheless, detailed findings for each analysis are presented below.

When compared with MND diagnosis among HIV+ participants ( $n = 29$ ), sensitivity values for error rates on the anti-saccade task were as follows: zero errors ( $n = 14$ ) on the task had a sensitivity of .483; one error ( $n = 3$ ) had a sensitivity of .586; two errors ( $n = 5$ ) had a sensitivity of .759; three errors ( $n = 3$ ) had a sensitivity of .862; four errors ( $n = 1$ ) had a sensitivity of .897; five errors ( $n = 2$ ) had a sensitivity of .966, and six errors ( $n = 1$ ) had a sensitivity of 1.000.

When compared with MND diagnosis among HIV+ participants ( $n = 29$ ), sensitivity values for task score on the anti-saccade task were as follows: a score of four ( $n = 25$ ) on the task had a sensitivity of 1.000; a score of three ( $n = 1$ ) on the task had a sensitivity of .138; a score of two ( $n = 2$ ) on the task had a sensitivity of .103; and a score of one ( $n = 1$ ) on the task had a sensitivity of .034.

When compared with HAD diagnosis among HIV+ participants ( $n = 3$ ), sensitivity values for error rates on the anti-saccade task were as follows: zero errors ( $n =$

1) on the task had a sensitivity of .333 and four errors ( $n = 2$ ) had a sensitivity of 1.000. No other rates of errors were recorded among the three participants.

When compared with HAD diagnosis among HIV+ participants ( $n = 3$ ), sensitivity values for task score on the anti-saccade task were as follows: a score of four ( $n = 1$ ) on the task had a sensitivity of 1.000 and a score of three ( $n = 2$ ) on the task had a sensitivity of .667. No other task scores were recorded among the three participants.

When considering MND and HAD diagnoses jointly to reflect a general diagnosis of some degree of HAND among HIV+ participants ( $n = 32$ ), sensitivity values for error rates on the anti-saccade task were as follows: zero errors ( $n = 15$ ) on the task had a sensitivity of .531; one error ( $n = 3$ ) had a sensitivity of .438; two errors ( $n = 5$ ) had a sensitivity of .281; three errors ( $n = 3$ ) had a sensitivity of .188; four errors ( $n = 3$ ) had a sensitivity of .094; five errors ( $n = 2$ ) had a sensitivity of .031, and six errors ( $n = 1$ ) had a sensitivity of zero.

When compared with diagnosis of some degree of HAND among HIV+ participants ( $n = 32$ ), sensitivity values for task score on the anti-saccade task were as follows: a score of four ( $n = 26$ ) on the task had a sensitivity of zero; a score of three ( $n = 3$ ) on the task had a sensitivity of .813; a score of two ( $n = 2$ ) on the task had a sensitivity of .906; and a score of one ( $n = 1$ ) on the task had a sensitivity of .969.

**Specificity of Anti-saccade Task.** The specificity of the anti-saccade task represents the proportion of HIV+ participants who have been classified as not having MND or HAD on the basis of their performance on neuropsychological measures that are also classified as not having MND or HAD on the basis of their performance on the anti-saccade task. This would be considered a desirable outcome in that the findings would be

congruent in showing the absence of significant impairment by both methods. In order to assess the specificity of the anti-saccade task, diagnoses of MND and HAD (both independently and collectively) were compared with error rates and task scores on the anti-saccade task. To briefly summarize the findings related to specificity, it appears that while fewer numbers of errors and corresponding higher scores on the task were associated with no diagnosis of MND and HAD in select cases, the small number of participants achieving anti-saccade scores suggestive of impairment and the uneven distribution of scores made these analyses largely insignificant and of little value. Detailed values for each analysis are presented below.

When compared with MND diagnosis among HIV+ participants ( $n = 29$ ), specificity values for error rates on the anti-saccade task were as follows: zero errors ( $n = 14$ ) on the task had a specificity of .481; one error ( $n = 3$ ) had a specificity of .423; two errors ( $n = 5$ ) had a specificity of .173; three errors ( $n = 3$ ) had a specificity of .077; and four or more errors ( $n = 4$ ) had a specificity of zero.

When compared with MND diagnosis among HIV+ participants ( $n = 29$ ), specificity values for task score on the anti-saccade task were as follows: a score of four ( $n = 25$ ) on the task had a specificity of zero; a score of three ( $n = 1$ ) on the task had a specificity of .923; while a score of one or two on the task ( $n = 3$ ) each had a specificity of 1.00.

When compared with HAD diagnosis among HIV+ participants ( $N = 3$ ), specificity values for error rates on the anti-saccade task were as follows: zero errors ( $n = 1$ ) on the task had a specificity of .487 and four errors ( $n = 2$ ) had a specificity of .038.



When compared with HAD diagnosis among HIV+ participants ( $N = 3$ ), specificity values for task score on the anti-saccade task were as follows: a score of four ( $n = 1$ ) on the task had a specificity of zero and a score of three ( $n = 2$ ) on the task had a specificity of .023.

When considering MND and HAD diagnoses jointly to reflect a general diagnosis of some degree of HAND among HIV+ participants ( $N = 32$ ), specificity values for error rates on the anti-saccade task were as follows: zero errors on the task had a specificity of .531; one error had a specificity of .592; two errors had a specificity of .857; three errors had a specificity of .959; and four or more errors had a specificity of 1.000.

When compared with diagnosis of some degree of HAND among HIV+ participants ( $N = 32$ ), specificity values for task score on the anti-saccade task were as follows: a score of four on the task had a specificity of 1.000; a score of three on the task had a specificity of .041; while a score of one or two on the task each had a specificity of zero.

### **Association between Anti-saccade Task and Performance on Other Cognitive Measures**

It was hypothesized that severe deficits in anti-saccade task performance would be associated with performance deficits on other measures of cognitive functioning among HIV+ individuals (see Tables 4 and 5 for summary information regarding performance on cognitive measures across groups). Because so few HIV+ participants showed significant deficits in anti-saccade performance, this hypothesis could not be adequately tested. To examine for the presence of any significant relationships that would be generally consistent with this hypothesis, Pearson correlation coefficients were

calculated between the anti-saccade error rates and task scores and neuropsychological test performance among HIV+ persons. It was found that only one neuropsychological test, Digit Symbol, had a significant relationship to both anti-saccade error rates,  $r(79) = -.254, p = .022$ , and task score  $r(79) = .274, p = .013$ . As would be expected given the hypothesis, greater deficits in anti-saccade task performance (i.e., more errors, resulting in a lower task score) were associated with poorer performance on Digit Symbol. An unanticipated finding was discovered in that Grooved Pegboard, non-dominant hand, had a significant relationship to the anti-saccade task score,  $r(79) = .237, p = .034$ , meaning that as time to complete Grooved Pegboard increased (signifying poorer performance), anti-saccade task score also increased. None of the other correlations between anti-saccade errors or task scores and neuropsychological measures were statistically significant among the HIV+ participants. These findings are reported in Table 6.

### **Additional Analyses**

To further explore any potential association between the anti-saccade task and other cognitive measures, Pearson correlation coefficients were calculated between anti-saccade task scores and error rates and scores on neuropsychological measures among all participants ( $N = 114$ ). These findings are presented in Table 6. The purpose of this analysis was to determine if performance on the anti-saccade task would be associated with impairment on neuropsychological measures in this community sample, regardless of HIV status. In this larger group, statistically significant correlations were found between Digit Symbol and both anti-saccade error rates,  $r(112) = -.235, p = .012$ , and task scores,  $r(112) = .241, p = .010$ . This was consistent with the researcher's expectations in that poorer performance on the anti-saccade was in fact associated with

lower scores on Digit Symbol. Once again, the unexpected finding of a statistically significant relationship between poorer performance on Grooved Pegboard, non-dominant hand, and higher scores on the anti-saccade task score was found, at  $r(112) = .237, p = .011$ . No other correlations, either in terms of error rates or task scores, were found to be statistically significant.

In order to better explore the finding that only ten of 81 HIV+ participants showed self-reported functional impairment on the CDS (four at the level associated with MND and six at the level representing HAD), some additional exploratory analyses were conducted. Given that participants were either younger than 40 or older than 49 as per the design of the parent study, the relationship of age to CDS was considered. The younger participants ( $n = 27$ ) showed a mean CDS score of 38.30 ( $SD = 33.70$ ), while the older participants ( $n = 54$ ) obtained a mean CDS of 38.46 ( $SD = 19.33$ ). While the mean scores were similar, a broader variance of self-reported scores among younger HIV+ individuals was noted. A correlation was also calculated between age and CDS for the entire HIV+ sample ( $n = 81$ ) and it showed a positive but negligible association,  $r(79) = .086, p > .05$ .

### **Discussion**

This exploratory research study sought to investigate the performance of HIV+ participants on the anti-saccade task, and how this performance might relate to cognitive functioning and diagnoses of MND and HAD. This exact relationship had not previously been examined in published literature. As one might expect with archival research, complications secondary to the archival data set provided some challenges and necessitated some changes in the methodology. Nonetheless, this exploratory research

provided some insight into the value of the anti-saccade task as a diagnostic tool, both in positive and negative findings.

### **Research Questions and Hypotheses**

In terms of the original two research questions, (a) how HIV+ individuals perform on the anti-saccade task and (b) how performance on the anti-saccade task relates to cognitive impairment and diagnoses of MND and HAD among HIV+ men and women, some challenges arose due to the exploratory nature of this archival research.

Performance on the anti-saccade task was manually recorded from filed records and analyzed by this writer and was not a specific focus of the parent study. After the anti-saccade data were analyzed for the present study, it appeared that variability and distribution of both error rates and anti-saccade task scores were severely limited with greater than half (50.6%) of HIV+ participants scoring zero errors on the measure (see Table 2), and more than nine out of ten (90.1%) achieving a score of 4 (see Table 3), the highest attainable on the task. No HIV+ participant scored more than 6 errors (out of 20 trials total), and only three (of 81) scored greater than 4 errors. Additionally, the medical and cognitive condition of the sample was unknown prior to the commencement of data analysis, and turned out to be better than expected overall based upon both participants' self-report of functional status and performance on the anti-saccade task. This was, in essence, a relatively healthy, well-functioning group based on those measures.

It was necessary to develop a method for classifying levels of HIV-associated neurocognitive disorders (HAND) after the data had been collected and coded. Informed by clinical and research guidelines (Antinori, 2007), diagnosis of MND was originally to be defined by (a) performance at least one, but less than two standard deviations beyond

the mean in at least two neuropsychological domains and (b) mild to moderate functional impairment, while HAD was to be defined by (a) performance at least two standard deviations beyond the mean in at least two neuropsychological domains and (b) significant functional impairment. However, once the scores on the Cognitive Difficulties Scale (CDS) were compared with neuropsychological test performance, the results were found to be largely incongruent. In general, participants in the parent study did not report a great deal of functional problems in their daily lives, as per the CDS. Specifically, there were 29 HIV+ participants who scored one SD beyond the mean on neuropsychological testing, while only four responded to a sufficient number of self-report items to indicate functional impairment on the CDS. Comparing these two outcomes, only two HIV+ participants would have reached criteria for MND taking into account both neuropsychological testing and the functional measure. Therefore, it was decided by the principal investigator (under advisement from a co-investigator of the parent study) to assign diagnoses of MND or HAD based on neuropsychological testing scores only. Using this approach, 29 HIV+ participants were assigned a diagnosis of MND and three participants met the criterion for HAD, for a total of 32 HAND diagnoses of the 81 participants (39.5%). However, given the lack of self-reported functional impairment among these participants, their assignment to categories of MND or HAD must be viewed as provisional at best.

In addition to the difficulties described above, determination of how performance on the anti-saccade task related to diagnoses of MND and HAD was somewhat thwarted by the participants' relatively good performance on the anti-saccade task itself. The most critical step in determining the predictive value of the anti-saccade task would have been

to compare HAND diagnosis using the anti-saccade task to HAND diagnosis using traditional means. This approach would require the creation of a cut-off point for diagnostic categories from continuous data, i.e., anti-saccade error rates and task scores in this study. These values are not intrinsic to the ROC analysis but are critically dependent upon the clinical context (Florkowski, 2008). The lack of variance and the generally good performance by HIV+ persons on the anti-saccade task made it impossible to determine clinically relevant cutoff scores for MND or HAD diagnosis using the anti-saccade task. An unanticipated finding of this research was that so many of the HIV+ persons in this sample performed within normal limits on the anti-saccade task. Because so many of the HIV+ participants performed well, there was diminished value in comparing diagnosis of HAND based on the anti-saccade task to traditional means of diagnosis. It appears that the anti-saccade task was not useful as an indicator of cognitive decline and HAND diagnoses among the participants represented in this specific data set. These circumstances therefore made it difficult to address the study's hypotheses.

A possible explanation of better-than-anticipated performance on the CDS as well the anti-saccade task is that the parent study sample seemed to be comprised of relatively healthy, well-functioning HIV+ individuals. As previously discussed in the literature review, the advent of HAART regimes has greatly improved the prognosis for HIV infection, and it appears that these participants were not experiencing a great deal of HIV-related cognitive or functional decline in their lives, perhaps due to these improved medical treatments, or potentially other unidentified factors.

It was also hypothesized that severe deficits in anti-saccade task performance would be associated with performance deficits on other measures of cognitive

functioning. Once again, the absence of any significant number of HIV+ persons with severe deficits in anti-saccade task performance made it difficult to address this hypothesis. Although the hypothesis could be said to have been unsupported by the lack of severe deficits in anti-saccade task performance, a series of correlations was calculated on an exploratory basis to determine what neuropsychological tests and domains would correlate with performance on the anti-saccade task. Among the HIV+ participants, performance on the anti-saccade task was significantly correlated with performance on Digit Symbol, which was represented in both the speed of information processing domain and the visuospatial domain, showing a significant relationship with performance on both the error rate (-.254) and task score (.274). These findings were consistent with the researcher's expectation that poorer performance on the anti-saccade would be associated with poorer performance on other neuropsychological measures among HIV+ individuals. Conversely, Grooved Pegboard, non-dominant hand, also had a significant relationship to anti-saccade task score (.237), but in the unexpected direction. Poorer performance on Grooved Pegboard, non-dominant hand, as reflected by greater time to complete the task, was associated with greater scores on the anti-saccade task, which represents better performance. Even though the correlation was modest, this finding was inconsistent with the researcher's general expectations for the data. Certainly more research is needed on the relationship of the anti-saccade task scores to Grooved Pegboard, non-dominant hand, before any conclusions can be drawing about the meaning of the association. None of the other correlations were statistically significant among the HIV+ participants, suggesting little overall association between the anti-saccade task and the other cognitive measures utilized in the study.

When looking at correlations between the anti-saccade task and other cognitive measures for the entire sample (see Table 6), a similar pattern was found as had been displayed among HIV+ individuals: Digit Symbol was significantly associated with both the anti-saccade error rate (-.235) and task score (.241). These results were consistent with the researcher's expectations. Once again, there was also the unexpected positive relationship between performance on the Grooved Pegboard, non-dominant hand, and the anti-saccade task score (.237). As noted earlier, more research is needed to confirm this unexpected association before any conclusions can be drawn. It is important to mention that because numerous correlations were calculated in the exploratory analyses, the possibility of obtaining significant associations simply by chance must be considered. Any significant findings obtained should therefore be viewed only as suggestive and as areas to be explored in future research.

### **Limitations of the Study**

Over the lengthy period of data collection in the longitudinal parent study, there have been changes to standards of care as the body of knowledge related to HIV has expanded. Specifically, diagnostic criteria and nomenclature for degrees of HIV-associated cognitive decline have been updated from AAN's 1991 standards to HNRC's 2007 standards. At the commencement of the current research, the data for the parent study had not been coded to reflect these changes, and as a result, decisions regarding appropriate diagnoses were made using informed clinical judgment. However, it is essential to note that without access to the participants or consultation with appropriately trained physicians, the diagnoses as determined can be considered no more than estimations of the participants' actual cognitive states. An additional limitation of this



research study is that the usefulness of the anti-saccade task was to be determined by comparison to neuropsychological and functional measures, and while these measures are considered fractional elements of the “gold standard” of diagnostic determination by current standards (McArthur et al., 2007), they do not provide absolute certainty in terms of diagnosis. Furthermore, due to unexpected findings within the data set, use of functional data was eliminated entirely when HAND-related diagnostic groups were created. Instead, the researcher had to rely solely on neuropsychological test performance, representing an even more narrow set of criteria and raising questions about whether diagnoses of MND and HAD were truly warranted. These limitations made it difficult to fully address the objectives of the present study.

The fact that functional impairment was determined solely through participant self-report in the present study represented another limitation. In an ideal design, the input of clinicians and collaterals would have been considered in determining levels of functional impairment. Doing so may have increased the likelihood that reliable data on levels of daily functioning would have been found. Alternatively, it is entirely possible that this sample represented a relatively healthy, well-functioning group where little functional impairment would have been found regardless of method. As it was not a focus of this study, it is unknown precisely what factors affected the functional status of these participants.

The archival nature of the current research also provides several limitations worth noting. While standardized test administration procedures were described in detail and adherence to these standards was documented in detail, no doubt some inconsistencies were present in the findings due to the nature of human error, especially among

individual administrations of the anti-saccade task, the measure of primary interest in this research. The researcher did not have the ability to independently determine the reliability of anti-saccade task administration or scoring. Further, many of the neuropsychological tests examined in this study have been updated to more recent editions in current clinical and research practice, but remained unchanged in the parent study to uphold consistency so there would be comparability between earlier and later participants. As was described in the Results chapter, the WAIS-R Digit Symbol subtest ended up being used to represent two different neuropsychological domains: speed of information processing and visuospatial skills. A research design that would have included less redundancy of measurement across these domains might have yielded additional information. Additionally, the domain of motor functioning was represented by only one test, Grooved Pegboard, non-dominant hand. Preferably, more than one test would be used to represent functioning in motor skills, and doing so may have provided supplementary information. Having additional measures available from the motor skills domain would have been especially valuable considering the unexpected positive relationship found between anti-saccade task scores and Grooved Pegboard, non-dominant hand performance.

Regarding the exclusionary criteria for participation, potential participants with advanced HAD were screened out of the parent study, due to concerns about their ability to complete the battery of neuropsychological measures. This was unfortunate as performance on the anti-saccade task by persons with HAD would have been most relevant to the current research study. Given the longitudinal design of the parent study, it is understandable why this exclusionary criterion was put into place, however, since the

present study examined only the first visit from each participant, access to anti-saccade and neuropsychological test performance on such participants would have been extremely valuable.

In summary, there were multiple limitations that were discovered during the analysis phase of the research, with some of the measures being quite challenging in terms of planned analysis due to an unexpected lack of variance. Specifically, the method by which diagnoses were to be determined, both by neuropsychological/functional means and by the anti-saccade measure, could not be fully accomplished when taking into account participant data. As a result, the predictive value of the anti-saccade task in terms of MND or HAD diagnosis was impossible to ascertain for this group of participants. Multiple potential reasons for this outcome exist, including the possibility that many of the HIV+ participants in the study were relatively healthy and free of the types of cognitive problems that the anti-saccade task is designed to assess. It is also possible that human error in the administration or scoring of the anti-saccade task led to inaccurate assessments. Because the anti-saccade task was administered by hand and by multiple individuals, the measure itself was not standardized beyond the general directions provided as instructions. If the study had included a greater number of participants diagnosed with any degree of HAND, and especially HAD, the study's hypotheses could have been more fully examined. Ultimately, if valid and reliable diagnoses of HAND existed at the origination of the parent study, and those participants had been diagnosed in real time by physicians consulting on their cases, it may have potentially been more reasonable to compare performance on the anti-saccade task with those firm diagnoses, assuming of course that a greater number of diagnoses would have

been given. With the present data set, and including measures such as the anti-saccade task and the self-report measure of functional impairment, it proved to be challenging to identify sub-groups of participants that could be reasonably and meaningfully compared on the dimensions of interest.

As with any sample-based research study, and particularly in a study with a relatively small  $N$ , the findings may not generalize well to the broader HIV+ population. The parent study also excluded HIV+ individuals who were between the ages of 40 and 49, which further limits generalizability. However, this study may produce some findings that will be useful to researchers as well as to health professionals engaged in diagnosing and treating HIV-associated cognitive decline.

### **Implications of Results and Directions for Future Research**

The current research was successful in demonstrating anti-saccade performance among HIV+ individuals in a community sample. Overall, low error rates were common and task performance was generally better than might have been expected. As a result, the second research question proved much more difficult to address. In fact, the findings were inconclusive overall in terms of the usefulness of the anti-saccade task as a screening measure for MND or HAD. The lack of findings within the current research does not preclude the possibility that the anti-saccade task may be of use in diagnosing HAND when administered and studied in a standardized, regulated manner, and when used among HIV+ patients who show more variance on the anti-saccade task. Additional research with perhaps less stringent exclusionary criteria in which HIV+ participants are diagnosed by neuropsychological testing, more comprehensive functional assessment (including both clinical and collateral ratings in addition to self report) and full medical

workup may provide more information about the usefulness of the anti-saccade task in diagnosing MND and HAD. Standardized administration of the anti-saccade task, perhaps administration by computerized means in lieu of hand administration, may also be a truer test of the measure. Significant correlations between performance on the anti-saccade task and Digit Symbol were intriguing and warrant further attention in future research. For the present study, Digit Symbol was used to represent the neuropsychological domains of visuospatial functioning and speed of information processing. The significant association with the anti-saccade suggests that the task may be useful as a screener for general neuropsychological decline, and further examination of the task may provide useful information.

The incongruence between the Cognitive Difficulties Scale and overall neuropsychological testing performance was an additional highlight of this research. While this was not a focus of study but rather an incidental finding, it remains an intriguing discovery that this self-report measure, often used as a screening measure to detect potential deficits in cognitive and motor skills, was largely not congruent with neuropsychological test performance. More research is needed on the relationship of self-reported functional assessment to cognitive and neuropsychological test performance among HIV+ persons. The findings of the present study suggest the need to incorporate multiple measures of functioning, rather than relying solely upon self report.

## **Conclusion**

In spite of the many complications and setbacks, it is the researcher's opinion that the time and effort put towards this research was constructive overall. The study succeeded in providing information about how an ethnically diverse sample of HIV+

individuals performed on the anti-saccade task, and a number of intriguing correlations between the anti-saccade task and other cognitive measures were identified. Certainly more research is needed to identify methods that will be useful in identifying and better understanding the cognitive challenges associated with HIV infection.

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Table 1

*Demographic Characteristics of Participants*

	Total ( <i>N</i> = 114)		HIV+ ( <i>n</i> = 81)		HIV- ( <i>n</i> = 33)	
	<i>N</i>	%	<i>n</i>	%	<i>n</i>	%
<b>Age</b>						
18 - 39	44	39	27	33	17	52
50+	70	61	54	67	16	48
Mean	47.03		48.35		43.76	
SD	12.27		11.68		13.21	
<b>Gender</b>						
Male	73	64	56	69	17	52
Female	41	36	25	31	16	48
<b>Ethnicity</b>						
African American	61	54	46	57	15	45
Hispanic	17	15	11	14	6	18
Caucasian	36	32	24	30	12	36
<b>Education</b>						
Mean	12.94		13.01		12.79	
SD	2.54		2.59		2.46	
<b>Handedness</b>						
Right	106	93	76	94	30	91
Left	8	7	5	6	3	9

Table 2

*Anti-Saccade Error Rates*

Number of Errors	0	1	2	3	4	5	6
All participants ( $N = 114$ )	65	7	24	8	6	3	1
HIV+ participants ( $n = 81$ )	41	6	18	8	5	2	1
HIV+, MND diagnosed ( $n = 29$ )	14	3	5	3	1	2	1
HIV+, HAD diagnosed ( $n = 3$ )	1	0	0	0	2	0	0
HIV+, HAND diagnosed ( $n = 32$ )	15	3	5	3	3	2	1
HIV- participants ( $n = 33$ )	24	1	6	0	1	1	0

Table 3

*Anti-Saccade Task Scores*

Score	4	3	2	1
All participants ( $N = 114$ )	104	6	3	1
HIV+ participants ( $n = 81$ )	73	5	2	1
HIV+, MND diagnosed ( $n = 29$ )	25	1	2	1
HIV+, HAD diagnosed ( $n = 3$ )	1	2	0	0
HIV+, HAND diagnosed ( $n = 32$ )	26	3	2	1
HIV- participants ( $n = 33$ )	31	1	1	0



Table 4

*Participant Performance on All Measures, Z-Scores*

Measure	All Participants ( <i>N</i> = 114)	HIV+ ( <i>n</i> = 81)	HIV- ( <i>n</i> = 33)
	Z-Score	Z-Score	Z-Score
Anti-saccade Error Rate	*	-0.12	0.28
Anti-saccade Task Score	*	-0.04	0.09
Cognitive Difficulties Scale	*	-0.13	0.31
Digit Span	0.28	0.18	0.54
Figural Visual Scanning Discrimination	0.73	0.91	0.31
Digit Symbol	-0.18	-0.21	-0.10
CVLT List A Immediate Recall	-0.03	0.20	-0.59
CVLT Long Delay	-0.47	-0.36	-0.76
Logical Memory II	0.43	0.42	0.45
Trail Making Test Part B	-0.71	-0.76	-0.58
Visual Reproduction Delay	-0.37	-0.46	-0.13
WCST Perseverative Errors	-0.04	-0.10	0.11
Stroop C	-0.17	-0.25	0.03
Boston Naming Test	-1.97	-1.97	-1.97
COWA FAS	-0.73	-0.74	-0.72
Category Fluency Animal Naming	-0.92	-0.98	-0.77
Block Design	-0.15	-0.21	-0.02

Table 5

*Participant Performance on All Measures, Means and Standard Deviations*

Measure	All Participants ( <i>N</i> = 114)		HIV+ ( <i>n</i> = 81)		HIV- ( <i>n</i> = 33)	
	Mean	SD	Mean	SD	Mean	SD
Anti-saccade Error Rate	1.08	1.47	1.30	1.53	0.67	1.26
Anti-saccade Task Score	3.86	0.47	3.85	0.50	3.91	0.38
Cognitive Difficulties Scale	35.41	23.90	38.40	24.83	28.06	19.95
Digit Span	10.89	3.24	10.57	3.31	11.67	2.97
Figural Visual Scanning Discrimination	69.45	25.55	71.56	28.77	64.27	14.00
Digit Symbol	9.46	2.64	9.36	2.75	9.70	2.38
CVLT List A Immediate Recall	51.54	9.73	51.00	10.54	52.85	7.34
CVLT Long Delay	11.04	2.99	11.06	3.25	10.97	2.27
Logical Memory II	60.32	29.21	59.31	29.79	62.82	28.00
Trail Making Test Part B	88.25	53.46	91.96	59.29	79.13	34.41
Visual Reproduction Delay	38.18	26.83	35.42	25.77	45.00	28.56
WCST Perseverative Errors	13.82	12.18	14.84	12.88	11.33	10.03
Stroop C	133.40	58.03	135.57	66.98	128.07	25.15
Boston Naming Test	49.06	8.43	48.91	9.01	49.42	6.91
COWA FAS	34.98	11.25	34.88	11.97	35.24	9.39
Category Fluency Animal Naming	17.02	4.71	16.53	4.15	18.21	5.78
Block Design	9.54	2.68	9.37	2.65	9.94	2.77
Grooved Pegboard	94.73	26.93	96.20	28.96	91.14	21.22

Table 6

*Pearson Correlations Between Neuropsychological Tests and Anti-saccade Task*

Measure	Anti-saccade Error Rate			Anti-Saccade Task Score		
	All Participants (N = 114)	HIV+ (n = 81)	HIV- (n = 33)	All Participants (N = 114)	HIV+ (n = 81)	HIV- (n = 33)
Digit Span	-.130	-.134	-.011	.132	.166	.157
Figural Visual Scanning Discrimination	.148	.164	-.068	-.145	-1.63	.208
Digit Symbol	-.235*	-.254*	-.138	.241**	.274*	.106
CVLT List A Immediate Recall	-.086	-.117	.069	.055	0.69	-.062
CVLT Long Delay	-.018	-.071	.051	.119	.184	-.080
Logical Memory II	.030	.049	-.028	-.085	-.084	-.095
Visual Reproduction	-.064	-.007	-.090	.099	.105	.058
Trail Making Test Part B	-.084	-.070	-.098	.101	.063	.237
WCST Perseverative Errors	-.111	-.103	-.107	.033	.020	.059
Stroop C	-.168	-.160	-.191	.173	.160	.293
Boston Naming Test	.048	.014	.170	.057	.107	-.125
COWA FAS	-.137	-.087	-.341	.152	.121	.285
Category Fluency Animal Naming	-.166	-.187	-.072	.164	.187	.096
Block Design	-.034	.001	-.068	.112	.097	.142
Grooved Pegboard	-.180	-.185	-.187	.237*	.237*	.248

\* Correlation is significant at .05 level

\*\* Correlation is significant at .01 level