CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

APATHY AND DEPRESSION AS PREDICTORS OF NEUROCOGNITIVE PERFORMANCE AND PSYCHOSOCIAL FUNCTIONING IN AN HIV-POSITIVE POPULATION

A thesis submitted in partial fulfillment of the requirements For the degree of Master of Arts in Psychology, Clinical Psychology

By

Kelsey Simpson

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The thesis of Kelsey Simpson is approved:

Gary Katz, Ph.D.  

Jill Razani, Ph.D.  

Alyssa Arentoft, Ph.D., Chair  

California State University, Northridge
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ABSTRACT

Apathy and Depression as Predictors of Neurocognitive Performance and Psychosocial Functioning in an HIV-Positive Population

By
Kelsey Simpson
Master of Arts in Psychology, Clinical Psychology

Apathy and depression are significant psychiatric disturbances observed in HIV infection. Although symptoms often overlap, recent evidence suggests that these two syndromes are dissociable in HIV. In the present study, we examined the associations between apathy, depression, cognition, and psychosocial functioning in 19 adults with HIV infection. All subjects completed a comprehensive neuropsychological battery, the Beck Depression Inventory- 2nd edition (BDI-II), and the Barkley Functional Impairment Scale-Self-Report (BFI-LF). The factor solution model of the BDI-II composed of factors representing Mood-Motivation (MM) disturbance and Self-Reproach (SR) was used to assess apathy and depression in this sample. These scales have not yet been examined using the revised version of the BDI (i.e., BDI-II), and have not yet been examined in relation to
psychosocial functioning in individuals with HIV. A series of bivariate correlations were performed to test the following hypotheses: 1) Apathy will be significantly associated with neuropsychological functioning, while depression will not, 2) higher scores on the Mood-Motivation disturbance (MM) scale of the BDI-II will be significantly associated with performance scores on measures of executive functioning and motor functioning, 3) the Self-Reproach (SR) scale of the BDI-II will not be significantly associated with neuropsychological functioning, 4) apathy will be significantly associated with psychosocial impairment while depression will not be significantly associated with psychosocial impairment, 5) the Mood-Motivation disturbance scale of the BDI-II will be significantly associated with BFIS-LF total impairment score, and 6) the Self-Reproach scale of the BDI-I will not be significantly associated with BFIS-LF total impairment score. These correlations showed depression (as measured by the SR factor) to be significantly associated with neurocognitive performance in learning and attention/working memory. Neither apathy nor depression were related to psychosocial functioning in this sample (BFIS-LF total impairment score); however, exploratory analyses revealed current depression severity to be associated with higher levels of impairment in functioning in activities in advanced educational/vocational settings. These results suggest that the presence of depression, particularly self-reproach, may signify greater HIV-associated CNS involvement among HIV+ individuals.
CHAPTER I

INTRODUCTION

Despite the success of combination antiretroviral therapy (CART) in dramatically improving immune health outcomes associated with HIV infection, neuropsychological impairment caused by HIV-associated CNS damage has continued to affect HIV+ individuals (NP; Woods et al., 2009). These impairments include declines in cognition, everyday functioning, disease progression, and other conditions in persons living with HIV (Heaton et al., 2011; Woods et al., 2009). Apathy and depression are significant psychiatric disturbances observed in HIV infection (Castellon et al., 1998, 2000, 2006; Hinkin et al., 1992; Kamat et al., 2012, 2013). Although symptoms often overlap, considerable evidence suggests that these two constructs are dissociable in HIV-infected populations (Kamat et al., 2012). Moreover, apathy ratings were not associated with depressed mood in HIV positive patients (Paul et al., 2005; Tate et al., 2003). This dissociation has also been observed in a variety of other neurological populations including Parkinson’s disease and Alzheimer’s disease (Kamat et al., 2012). Imaging studies across neurological populations (including patients with HIV) report that left prefrontal and limbic system dysregulation is associated with depression, and medial prefrontal and deep subcortical pathology is associated with apathy (Paul et al., 2005; Starkstein et al., 1992). Thus, apathy and depression are considered to be mood disturbances that can occur alone and concurrently in HIV infection.

Evidence suggests that apathy and depression are independently associated to cognitive performance and everyday functioning in patients with HIV (Castellon et al., 2006; Kamat et al., 2012, 2013). For example, in a study that examined the role of apathy
and depression in predicting everyday functioning disability in a sample of HIV-positive patients in Brazil, levels of apathy and not depression significantly predicted deficits on instrumental activities of daily living in the domains of work, grocery shopping, social activities, and housekeeping (IADLs; Kamat et al., 2012). In a study that used a principal component analysis to factor analyze items on the Beck Depression Inventory (BDI) to examine the relationship between factors representing apathy, somatic complaints, and negative cognitions and neuropsychological performance in patients with HIV, apathy severity significantly associated with impairment on measures of verbal memory, executive functioning, and motor speed in patients with HIV; while all other symptoms of depression did not (Castellon et al., 2006). Although this evidence suggests that apathy and depression may differentially contribute to important cognitive and functioning outcomes in HIV, research in this field is sparse. In addition, the studies available have utilized a variety of different methods to measure these syndromes, such as diagnostic interviews, self-report scales, and/or previous diagnostic history; thus, the specific role of apathy in HIV remains unclear (Castellon et al., 2006; Kamat et al., 2013). To address these issues, the main objective of this study was to further investigate the relationship between these important HIV-associated psychiatric disturbances, and NP performance as well as everyday functioning in patients with HIV.

**Literature Overview**

The literature review that follows will describe the neuropathology of HIV/AIDS, including the mechanisms by which HIV enters the brain and causes central nervous system damage. It will also discuss the link between pathological changes in the brain associated with HIV and changes in neuropsychological functioning in patients with HIV.
HIV-associated neurocognitive disorders (HAND) will be defined and the current diagnostic criterion and prevalence rates associated with the three current classifications of HAND will be discussed. In addition, this review will describe the relationship between HIV-related neuropathology and declines in everyday functioning, provide empirical evidence of the real-world implications of such deficits, and highlight the continued need for research examining psychosocial functioning in this population. Lastly, this review will describe the neurocognitive and functional consequences of depression and apathy in patients with HIV/AIDS, and provide empirical evidence highlighting the distinctiveness and importance of these two constructs in the context of HIV.
CHAPTER II
REVIEW OF LITERATURE

HIV Background and Statistics

The human immunodeficiency virus (HIV) is a retrovirus that attacks and destroys CD4 T-cells in the body’s immune system (CDC, 2013). According to the Center for Disease Control and Prevention, approximately 1.2 million individuals in the Unites States and 35 million individuals worldwide are infected with HIV (CDC, 2013). Incidence rates have stabilized in the last few years at around 50,000 new diagnoses per year in the U.S. (CDC, 2013).

Neuropathology of HIV/AIDS

The central nervous system (CNS) is a major target for HIV infection (Hult et al., 2008). Early in the course of infection, the human immunodeficiency virus (HIV) infects macrophages and lymphocytes (Anthony & Bell, 2008; Hult et al., 2008). Two views have been postulated concerning the mechanism by which the virus enters the blood brain barrier (BBB; Anthony & Bell, 2008; Hult et al., 2008). The “Trojan horse” theory suggests that infected monocytes cross the endothelium and settle as infected perivascular macrophages (Hult et al., 2008). Macrophages may then replicate the virus through cell-to-cell contact with microglia cells (Anthony & Bell, 2008; Hult et al., 2008). The alternative route into the BBB is by way of a single CD4- cell-independent entrance (Ances & Clifford, 2008; Hult et al., 2008).

Once HIV enters the CNS, severe pathology can ensue due to a variety of direct (e.g. viral proteins) and indirect (e.g. inflammatory) mechanisms (Hult et al., 2008). For example, in response to HIV’s entry into the CNS, pro-inflammatory cytokines (e.g.
TNFα) are released to facilitate the opening of paracellular routes (Hult et al., 2008). Due to the accumulation of leukocytes within the parenchyma, this results in severe inflammation and neurotoxic damage (Hult et al., 2008). Overall, repeated exposure to viral proteins and enhanced viral replication within the CNS prompts a cascade of neurotoxic events that can lead to substantial neuronal dysfunction and loss (Ances & Clifford, 2008).

Pathological changes associated with HIV-related CNS damage have been found to affect a variety of different regions of the brain; however, the most common structural changes occur in the frontostriatal circuits involving the basal ganglia, as well as the frontosubcortical white and gray matter (Cotter & Everall, 1996; Woods et al., 2009). Neuronal injury in these regions has been linked to HIV disease severity (e.g. low nadir CD4 levels, and AIDS status), neurocognitive impairment, and functional impairment (Jernigan et al., 1993).

**HIV and Cognition**

Cognitive compromise is considered to be the most common consequence of HIV-associated CNS damage (Ances & Clifford, 2008). Evidence from neuropathological, neuropsychological and in-vivo imaging studies find that disruptions in frontostriatal circuitry are associated with a spectrum of deficits ranging from subtle cognitive impairments to profound cases of dementia in some patients (Heaton, 2010). The most common deficits occur in the areas of motor and information processing speed, executive functioning, attention, and working memory (NP; Woods et al., 2009). Neurocognitive impairments are not universal among HIV infected patients; however, signs and symptoms of at least mild neurological dysfunction are seen in approximately
one-third to one-half of individuals living with HIV/AIDS (Heaton, 2010; Woods et al., 2009). Unlike other neurodegenerative diseases such as Alzheimer’s and Huntington’s disease, the course of cognitive change in HIV is not always progressive (Woods et al., 2009). In fact, it is highly unpredictable, and changes have been found to occur in patterns of stability, fluctuation, progression, and even regression in some cases (Ances & Clifford, 2008). Nonetheless, cognitive decline is widely prevalent in HIV, and some patients develop a condition known as an HIV-associated neurocognitive disorder (HAND; Heaton, 2010).

**HIV-Associated Neurocognitive Disorders (HAND)**

HIV-associated neurocognitive disorders are diagnoses given to HIV infected individuals who exhibit neurocognitive impairment that is not thought to be caused primarily by other factors such as comorbid medical conditions or severe substance abuse (HAND; Gisslén, Price & Nilsson, 2011). These conditions are seen more frequently in advanced stages of HIV disease (e.g. AIDS), but can also occur in individuals with medically asymptomatic, and symptomatic HIV infection (Heaton, 2010; Woods et al., 2009).

**Diagnosis**

The current classification system used to diagnose NP impairments in HIV was created in 2007 by the National Institutes of Mental Health (Antorini et al., 2007). According to these diagnostic guidelines, HIV infection can induce NP impairments that result in three potential HAND diagnoses: asymptomatic neurocognitive impairment, HIV-associated mild neurocognitive disorder and HIV-associated dementia (ANI, MND, HAD; Antorini et al., 2007). ANI is diagnosed in individuals who exhibit
neuropsychological impairment in at least two cognitive domains, but who do not exhibit significant impairments on functional tasks or do not report impairment in activities of daily living (Gisslén, Price & Nilsson, 2011). MND requires mild-to-moderate neurocognitive impairment within two or more cognitive domains resulting in at least mild changes in everyday functioning (Robertson et al., 2007). HAD requires moderate-to-severe cognitive impairment in at least two cognitive domains coupled with moderate-to-severe impairment in everyday functioning (Robertson et al., 2007).

**Functional Impact of HIV**

In addition to impairments in cognition, HIV-infection has also been linked to deficits in everyday functioning in patients with HIV (Heaton et al., 2004). These impairments are observed in basic activities of daily living (e.g., bathing, dressing) and more complex activities of daily living known as instrumental activities of daily living (e.g., financial management, cooking) (Heaton et al., 2004; Hinkin et al., 2004). Although profound declines in basic functioning on simple tasks in everyday are less frequently observed in the post-CART era, impairments on more complex instrumental activities of daily living remain a significant concern in this population (Heaton et al., 2004). The most typical IADL deficits affect everyday functioning in the areas of money management, vocational skills, cooking, shopping, and medication adherence (Heaton et al., 2004; Gorman et al., 2009).

At present, the available studies concerning the functional impact of HIV-related NP deficits have utilized various questionnaires and gross measures of functional ability to evaluate the real-world consequences of HIV-infection (Heaton et al., 2004). These include measures such as the Activities of Daily Living scale, Patient’s Assessment of
Own Functioning Inventory (PAOFI), and criterion-referenced functional tasks designed to measure competence in medication management, cooking, shopping, and vocational performance (Heaton et al., 2004). While prior data illustrate that HIV-related NP deficits significantly impact the ability to carry out activities required for independent living, the functional consequences of HIV-related NP impairment on psychosocial activities of daily living has not yet been looked. As HIV has transformed from a fatal illness into a chronic disease in the post-CART era, patients with HIV are living longer, which raises important questions about specific HIV-associated functional deficits (Heaton et al., 2004). Thus, further research is needed in this field to advance our understanding of HIV-related deficits in functioning in this patient population.

**Depression in HIV**

HIV infection is commonly accompanied by a variety of psychiatric disturbances (Castellon et al., 2006). The most prevalent and widely studied complication in HIV is depression (Castellon et al., 2006). The prevalence of Major Depressive Disorder (MDD) in HIV-infected cohorts is reported to be between 40-60%, and the incidence is reported to be approximately 10% over an average two-year period (Cysique et al., 2007). Symptoms of depression are elevated among HIV-positive populations (Castellon et al., 2006; Ciesla & Roberts, 2001). HIV-associated CNS involvement and MDD have also been found to share similar frontostriatal pathology; however, studies examining the neuropathogenesis of MDD in individuals with HIV yield mixed results (Castellon et al., 1998; Kamat et al., 2012). In a cohort of HIV+ patients, those with elevated ratings of depression showed bilateral alterations of the ventral tegmental region, nucleus accumbens, and globus pallidus (Stubbe-Drager et al., 2012). Similarly, HIV-infected
adults with depression displayed altered white matter integrity in the right anterior cingulate and left thalamus (Smith et al., 2008). However, additional studies have failed to find an association between depression and frontostriatal pathology in similar cohorts (Paul et al., 2005). Furthermore, in current HIV literature, depression is considered to be a possible consequence of HIV-related CNS disruption and a common comorbid mood disturbance found in HIV-infected patients (Ciesla & Roberts, 2001).

**Depression and Everyday Functioning**

Depression in patients with HIV has been linked to profound declines in everyday functioning (Castellon et al., 2006; Heaton et al., 2004). In a study that examined the relationship between depression and self-report measures of functioning on activities of daily living (ADLs), higher depression scores were found among those who reported impairments in medication management, driving, and cognition in HIV patients (Thames et al., 2011). Similarly, depression severity was significantly associated with vocational difficulties and medication non-adherence in an HIV-positive cohort (Bogart et al., 2000). It has been noted that proper diagnosis and treatment of depression has led to significant increases in everyday functioning in persons with HIV suggesting that impairments due to affective symptoms may be reversible (Nanni et al., 2015). This highlights the importance of considering depression when diagnosing cases of HAND and predicting deficits in everyday functioning in persons living with HIV.

**Depression and Cognition**

Depression has been linked to neurocognitive comprise in a number of different neurologic and psychiatric populations (Burt, Niederehe & Zembar, 1995; Cassens, Wolf & Zola, 1990). However, the vast majority of studies in HIV literature have found the
neurocognitive and psychiatric sequelae of HIV/AIDS to be largely independent of one another (Castellon et al., 2006; Cystique et al., 2007). For example, in a longitudinal study of over 270 HIV+ patients, group comparisons revealed no neurocognitive performance differences in patients with depression verses patients without depression (Cystique et al., 2007). Most studies that have failed to find an association between depression and cognition in HIV have failed to recognize the multidimensionality of depression, and the fact that symptoms may manifest differently in the context of HIV (Castellon et al., 1998, 2000, 2006).

The Beck Depression Inventory (BDI), one of the most widely used self-report measures for assessing depression among the general population, frequently serves as an index of depressive symptoms in research with HIV-infected samples (Castellon et al., 2006). However, the BDI was originally constructed as a diagnostic tool for discriminating between depressed and non-depressed psychiatric patients (Beck, 1987). Moreover, the degree to which symptoms of depression may manifest differently in primary psychiatric versus primary neurologic populations has not yet been sufficiently studied (Castellon et al., 2006). In fact, only a handful of studies have explored the factor structure of the BDI among HIV samples (Castellon et al., 2006). Nevertheless, these studies have consistently found two- and three-factor solutions of depressive symptoms using both exploratory and confirmatory factor analyses (Hobkirk et al., 2015; Kagee, Nel & Sal, 2014). For example, Kagee, Nel, and Saal (2014) found a three-factor solution of cognitive, affective, and somatic symptoms of depression to represent the neuropsychiatric manifestation of depressive symptoms in a sample of 185 HIV-positive patients (Kagee, Nel & Sal, 2014).
In a study that examined the factor structure of the BDI and the relationship between components of depression and neuropsychological performance in patients with HIV, Castellon et al., (2006) produced a three-factor solution model comprised of symptoms involving negative cognitions, somatic complaints, and mood-motivation disturbances (Castellon et al., 2006). These three factors differentially associated with neurocognitive performance in his study (Castellon et al., 2006). Moreover, mood-motivation disturbances significantly associated with impairment on measures of verbal memory, executive functioning and motor speed, while negative cognitions and somatic disturbances did not (Castellon et al., 2006). These findings suggest that certain dimensions of depression may be more accurate indicators of neurocognitive impairments in individuals with HIV than others (Castellon et al., 2006).

Apathy

The definition of apathy is the overt diminution in goal-directed behaviors and the initiation of cognitive, emotional and motoric activities (Marin, 1991). Common behavioral manifestations of apathy include: feelings of indifference, loss of interest or pleasure in formerly enjoyable activities, and reductions in self-directed thought content (Marin, 1991). Although symptoms of apathy frequently overlap with symptoms of depression, apathy is considered to be a distinct psychiatric syndrome that can occur independently and concurrently with depression in different patient populations (Rabkin et al., 2000). Moreover, symptoms of apathy are not required to be accompanied by changes in appetite, sleep disturbance, recurrent thoughts of death/suicide, fatigue, or psychomotor agitation that exist in depression (Marin, 1991). Neuropathological imaging studies across a variety of neurologic populations (including patients with HIV), have
found that depression was associated with left prefrontal and limbic system
dysregulation, and apathy to be driven by medial prefrontal, anterior cingulate and deep
subcortical pathology, further supporting the discriminant validity of these two constructs
(Kamat et al., 2012; Starkstein et al., 1992). This evidence suggests that apathy may be a
unique marker of CNS disruption in patients with neurologic conditions.

**Apathy in HIV**

Although apathy has been recognized in general medical literature as a common
neurobehavioral disturbance associated with diseases including schizophrenia,
Alzheimer’s disease, Parkinson’s disease, and Huntington’s disease, only in the past
decade has apathy been considered an important neuropsychiatric symptom of HIV
(Kamat et al., 2012; Rabkin et al., 2000; Starkstein et al., 1992). Approximately 30-50%
of HIV-infected individuals are found to exhibit elevated symptoms of apathy (Kamat et
al., 2012). The presence and severity of apathy symptoms have been found to be largely
unrelated to HIV disease severity factors including CD4 cell counts, RNA viral load
levels, and AIDS status (Castellon et al., 1999, 2000; Rabkin et al., 2000). However,
symptoms of apathy have been associated with NP impairments in cognition and
everyday functioning in HIV-infected cohorts (Barclay, Hinkin & Castellon, 2007;
Castellon et al., 1998, 2000; Paul et al., 2005; Tate et al., 2003).

**Apathy and Cognitive Performance**

The current body of literature suggests that symptoms of apathy are significantly
associated with neurocognitive impairments in patients with HIV (Castellon et al., 2000,
2006; Kamat et al., 2012; Paul et al., 2005). For example, Paul et al., (2005) found
symptoms of apathy to be correlated with poor performance on neurocognitive tests in
verbal and nonverbal episodic memory, and cognitive set switching in patients with HIV (Paul et al., 2005). Similarly, Castellon et al., (2000) found apathy and not depression to be a significant predictor of deficits in learning efficiency, executive functioning, cognitive flexibility, and episodic memory in an HIV-infected cohort (Castellon et al., 2000). However, other studies have reported non-significant relationships between apathy and cognitive impairment in individuals with HIV. Rabkin et al., (2000) did not find an association between ratings of apathy and neurocognitive performance in an HIV-infected cohort (Rabkin et al., 2000). One potential explanation for these inconsistent findings may be a matter of methodological differences. The available studies in this field have utilized a variety of assessment tools to measure apathy; thus, the specific role of apathy in predicting deficits in neurocognitive performance has not been well established in the context of HIV-infection.

**Apathy and Everyday Functioning**

Apathy has been linked to impairments on activities of daily living, diminished quality of life, increased burden to caregivers, decreased general health, and poor treatment compliance in patients with Alzheimer’s and Huntington’s disease; however, much remains unknown about the real-world correlates in patients with HIV (Castellon et al., 2006). In a recent study conducted on 75 patients with HIV in Brazil, Kamat et al., (2012) found higher levels of self-reported apathy to be associated with greater severity of total IADL decline (Kamat et al., 2012). Similarly, Barclay, Hinkin & Castellon (2007) found apathy to be associated with poor self-reported medication adherence in patients with HIV (Barclay, Hinkin & Castellon, 2007). Although these findings illustrate that apathy may play a considerable role in predicting impairments in everyday functioning in
persons with HIV, research in this field is limited. In addition, the potential role of apathy in predicting specific impairments in psychosocial daily life activities has not been looked at. Given the high prevalence of apathy in HIV, further research is needed in this field to enhance our understanding of specific functioning deficits associated with this HIV-related CNS damage.


The Barkley Functional Impairment Scale: Self-Report (BFIS-LF) was used to evaluate psychosocial functioning in this study. The distinction of the BFIS-LF compared to previous assessment measures used to measure functioning ability is that it allows clinicians to focus specifically on psychosocial dysfunction (Barkley, 2011). This specific component of behavior has not been thoroughly examined in patients with HIV. The BFIS-LF is a 15-item self-report rating scale designed to evaluate functional deficits in daily life activities across 15 major psychosocial domains including: home-family, home-chores, work, social-strangers, social-friends, community activities, education, marriage/cohabiting/dating, money management, driving, sexual relations, daily responsibilities, self-care routines, health maintenance and childrearing (Barkley, 2011). The BFIS-LF demonstrates high internal consistency (Cronbach’s alpha of .97) and test-retest reliability when administered over a 2-3 week time interval (.72 for the total impairment score; Barkley, 2011).

**Rationale for Proposed Study**

The primary objective of this study was to examine the relationship between apathy, depression, neurocognitive performance, and psychosocial functioning in an HIV positive population. While previous findings together elucidate to some degree the
neurocognitive and functional mechanisms of apathy and depression in HIV, methodological differences involving the measures used to evaluate these two constructs impose major threats to the external validity of the literature. To address this issue, we plan to use the factor solution model created by Castellon and colleagues (2006) to investigate the relationship between symptoms of apathy, depression, neuropsychological performance and psychosocial functioning in an HIV-positive sample. These scales have not yet been examined using the revised version of the BDI (i.e., BDI-II), and have not yet been examined in relation to psychosocial functioning in HIV (Castellon et al., 2006; Kamat et al., 2012). The results of this study will hopefully enhance the clinical utility of the BFIS and BDI in treating and screening for cognitive and functional impairments in this population.

**Hypotheses**

1) Apathy will be significantly associated with neuropsychological functioning, while depression will not be significantly associated with neuropsychological functioning.
   a. Higher scores on the Mood-Motivation disturbance (MM) scale of the BDI-II will be significantly associated with worse performance on measures of executive functioning and motor functioning.
   b. The Self-Repooch (SR) scale of the BDI-II will not be significantly associated with neuropsychological functioning.

2) Apathy will be significantly associated with psychosocial impairment while depression will not be significantly associated with psychosocial impairment.
a. The Mood-Motivation disturbance (MM) scale of the BDI-II will be significantly associated with BFIS-LF total impairment score.

b. The Self-reproach (SR) scale of the BDI-II will not be significantly associated with BFIS-LF total impairment score.
CHAPTER III  
METHODOLOGY

Participants

Nineteen HIV+ individuals were recruited through local HIV clinics and self-referral, and were seen at the University of California, Los Angeles as part of a larger study examining changes in white matter integrity and neuropsychological functioning as a result of HIV medication (R25 MH080663-06 0253-6142-4609; PI: A. Arentoft). To be included in the study, participants had to be HIV+ (tested by enzyme-linked immunosorbent assays (ELISA) and confirmed by Western Blot), at least 18 years of age, English-speaking, born within the United States, completed at least 6 years of formal education, identified as African American or non-Hispanic white, currently taking HIV antiretroviral medications, and had a viral load < 5000 at the time of the research study. Participants were excluded if they were diagnosed with severe psychiatric illness (i.e., schizophrenia, schizoaffective disorder, bipolar disorder, or other psychotic disorder, or substance dependence) within the last year, or had a history of a significant neurological condition (i.e., epilepsy/seizure disorder; cerebrovascular accident; CNS-opportunistic infection such as toxoplasmosis, encephalitis, neoplasm, or progressive multifocal leukoencephalopathy). This study was approved by the UCLA institutional review board (IRB). All participants provided informed consent and were compensated for their participation.

Measures

Neuropsychological assessment
Participants completed a battery of neuropsychological tests, administered by trained psychometrists. All measures are discussed in more detail below. Raw scores were converted to demographically $T$-scores using appropriate norms (see Table 1). Individual test $T$-scores were averaged within domain to generate domain NP $T$-scores. The Global NP $T$-score was obtained by averaging all individual test $T$-scores. Functioning was assessed in the following domains using the following measures:

1. Attention/working memory (Wechsler Adult Intelligence Scale 4th Edition-Letter Number Sequencing)

2. Executive functioning (Trail Making Test—Part B, Stroop Color-Word Test-Interference score)

3. Learning (Hopkins Verbal Learning Test-Revised (HVLT-R)-Total Recall, Brief Visuospatial Memory Test-Revised (BVMT-R)-Total Recall)

4. Memory (HVLT-R Delayed Recall, BVMT-R Delayed Recall)

5. Motor functioning (Grooved Pegboard-Dominant hand-total time; non-dominant hand-total time)

6. Processing speed (WAIS-IV Digit Symbol, WAIS-IV; Symbol Search Trail Making Test—Part A)

7. Verbal fluency (Controlled Oral Word Association Test [F-A-S; Animals])

*Stroop Color Word Interference Test.* The Stroop Color Word Interference Test assesses multiple functions including: color naming, word reading speed, sustained attention, selective attention, and, in the interference condition, selective attention and the
ability to inhibit a habitual response in favor of a more overlearned response (Trenerry, Crosson, Deboe, & Leber, 1989). The dependent variables of interest in this measure include the number of words named correctly in 45 seconds and the number of errors on three separate trials. This test has been found to be highly reliable and moderately valid when compared to other versions of the test (e.g. Victoria version; Trenerry, Crosson, Deboe, & Leber, 1989).

Trail Making Test, parts A & B (TMT). The Trail Making Test is used to assess visual-motor functioning, attention, psychomotor speed, and conceptual switching. Trails A requires subjects to connect numbers in ascending order as quickly as possible without making mistakes (Reitan, 1969). Trails B requires subjects to switch between connecting numbers and letters in an ascending sequence (Reitan, 1969). The outcome variable in both tasks is completion time in seconds and total number of errors on each trial.

FAS (Controlled Oral Word Association Test). The FAS test assesses semantic and phonemic verbal fluency over the course of three one-minute trials (Benton, Hamsher, Varney & Spreen, 1983). In all three trials the subject is asked to name as many words as he/she can starting with a given letter of the alphabet (“F”, “A”, and “S”). The dependent variable of interest produced in this task is the total number of words produced (Benton, Hamsher, Varney & Spreen, 1983). Animals. The Animals test assesses semantic fluency by requiring the examinee to name as many animals as they can within a one-minute interval. The dependent variable in this measure is total number of correct words (Spreen & Strauss, 1998).

Grooved Pegboard. The Grooved Pegboard test measures motor speed and dexterity of upper extremity fine motor movements (Lezak, 1995). Subjects are required
to rapidly place small metal pegs, which require substantial manipulation, into their respective holes. This test is administered in two different trials, one using only the subject’s dominant hand and the other with the non-dominant hand. The dependent variable of interest is completion time in seconds (Lezak, 1995).

*Letter-Number Sequencing.* This subtest from the Wechsler Adult Intelligence Scale-4\(^{th}\) edition (WAIS-IV) test measures working memory by verbally presenting the examinee with a series of numbers and letters that increase in quantity every three trials. The examinee must then reorganize the numbers and letters into ascending numerical and alphabetical order. The score is calculated by summing the total number of items completed correctly (Wechsler, 1987).

*Digit Symbol Coding.* This subtest from the WAIS-IV measures processing speed, working memory, visual scanning, and visual motor coordination (Wechsler, 1987). Subjects are required to rapidly copy symbols that are paired with numbers within 120 seconds. The dependent variable of interest is the total number of symbols accurately transcribed.

*Symbol Search.* This subtest from the WAIS-IV measures mental proficiency, visual scanning, processing speed, short-term visual memory and visual-motor coordination (Wechsler, 1987). Subjects are required to scan a search group and indicate whether one of the symbols in the target group matches within a specific time limit. Outcome is measured using the number of correctly identified symbols.

*Hopkins Verbal Learning Test-Revised (HVLT-R).* The HVLT-R test measures verbal learning and memory (Brandt & Benedict, 2001). The subject is presented with a 12-item word list comprised of 3 semantic categories, and their ability to recall list words
is tracked over three trails. Approximately 20 to 25 minutes after the first three trials are administered, delayed recall and recognition trials are completed. The delayed recall trial requires the examinee to freely recall any of the words on the list, and the recognition trial asks the subject to correctly distinguish words on the original list from 6 semantically-related and 6 semantically-unrelated distracters (Brandt & Benedict, 2001). Multiple dependent variables of interest are yielded from this task, including the total number of words recalled on trials 1-3 (i.e., learning), total words recalled on the delayed recall trial (i.e., long-term recall memory), and the total number of items recognized (i.e., long-term recognition memory; Brandt & Benedict, 2001).

Brief Visual Memory Test-Revised (BVMT-R). The BVMT task measures non-verbal learning and memory by assessing the immediate and delayed recall of six geometric designs (Benedict, 1997). The subject is presented with 6 figures, and their ability to transcribe the figures accurately and in their correct location on the page is tracked over multiple trials. Like the HVLT-R, the BVMT-R produced Total Recall, Delayed Recall, Percent Retained, and Recognition Discrimination indices.

Mood Assessment

The factor solution model of the original Beck Depression Inventory, originally comprised of the Mood-Motivation disturbance (MM), Self-Reproach (SR), and Somatic Disturbance (SOM) scales, was used to measure symptoms of apathy and depression in this study. This model was created by Castellon et al., (2006), using a principal component analysis with orthogonal rotation (Castellon et al., 2006). The most recent version of the BDI, the Beck Depression Inventory-2nd edition (i.e. BDI-II) was used in this study. The BDI-II is a widely used self-report rating scale containing 21 questions
pertaining to the presence and intensity of various symptoms and signs of depression over
the past two weeks (Beck, Steer & Brown, 1996). Due to revisions from BDI to BDI-II,
two items that previously belonged to the Somatic disturbance (SOM) scale in Castellon
et al.’s model were no longer included in the newest version of the BDI. Thus, our study
only utilized the Mood-Motivation disturbance and Self-Reproach factor scales in which
items remained constant across both self-report versions. Reliability estimates for the
Self-Reproach and Mood-Motivation disturbance scales are reported to be acceptable
(Cronbach’s alpha coefficient greater than .75) (Castellon et al., 2006).

Factor scale scores in this study were obtained by calculating the sum of scores on
items that loaded onto these factors in Castellon et al.’s original model. The Mood-
Motivation disturbance (MM) scale included BDI-II: Item 1 (Sadness), Item 4 (Loss of
pleasure), Item 17 (Irritability), Item 12 (Loss of interest), Item 13 (Indecisiveness), Item
15 ( Decreased initiative/loss of energy), and Item 20 (Tiredness/fatigue) (Castellon et
al., 2006). The Self-Reproach (SR) scale included: Item 2 (Pessimism regarding future), Item
3 (Past failure), Item 5 (Guilty feelings), Item 6 (Sense of punishment), Item 7 (Self-
dislike), Item 8 (Self-criticalness), Item 9 (Suicidal ideation), and Item 10 (Crying).

**Psychosocial Functioning Assessment**

Functional Impairment Scale: Self-Report, is a 15-item self-report rating scale designed
to evaluate functioning deficits in daily life activities across 15 major psychosocial
domains on adults between the ages of 18 and 89 years old (Barkley, 2011). Psychosocial
domains assessed include: home-family, home-chores, work, social-strangers, social-
friends, community activities, education, marriage/cohabiting/dating, money
management, driving, sexual relations, daily responsibilities, self-care routines, health maintenance and childrearing (Barkley, 2011). Scores on each item range from 0 (Not at all) to 9 (Severe), and participants can indicate that a specific domain does not apply to them. Dependent variable of interest in this measure is total impairment score (i.e., sum of all domain scores, excluding any marked as “not applicable”). The BFIS demonstrates high internal consistency (Cronbach’s alpha of .97) and test-retest reliability when administered over a 2-3 week time interval (.72 for the total impairment score; Barkley, 2011).

Table 1

Neuropsychological Battery and Normative Data

<table>
<thead>
<tr>
<th>Domain</th>
<th>Neuropsychological Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processing speed</td>
<td>• WAIS-IV- Symbol Search (Wechsler, 1997)</td>
</tr>
<tr>
<td></td>
<td>• WAIS-IV- Coding (Wechsler, 1997)</td>
</tr>
<tr>
<td></td>
<td>• Trailmaking Test - Part A (Robert K. Heaton, Miller, Taylor, &amp; Grant, 2004)</td>
</tr>
<tr>
<td></td>
<td>• Brief Visuospatial Memory Test-Revised (BVMT-R) (R. Benedict, 1997)</td>
</tr>
<tr>
<td>Attention/Working Memory</td>
<td>• WAIS-IV-Letter-Number Sequencing (Wechsler, 1997)</td>
</tr>
<tr>
<td>Motor functioning</td>
<td>• Grooved Pegboard Test (Heaton, Miller, Taylor, &amp; Grant, 2003)</td>
</tr>
<tr>
<td>Executive functioning</td>
<td>• Trailmaking Test - Part B (Robert K. Heaton, Miller, Taylor, &amp; Grant, 2004)</td>
</tr>
<tr>
<td></td>
<td>• Stroop Color-Word Test (Golden, 1978)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>• Controlled Oral Word Association Test (FAS)</td>
</tr>
<tr>
<td></td>
<td>• Animals Test (Heaton, Miller, Taylor, &amp; Grant, 2003)</td>
</tr>
</tbody>
</table>
Memory

- Brief Visuospatial Memory Test-Revised (BVMT-R) (R. Benedict, 1997)

Data Analysis

The Statistical Package for the Social Sciences, Version 22.0 (2013) was used for all statistical analyses. Bivariate correlations were computed to assess the relationship between BDI-II factor scales, psychosocial functioning, and neurocognitive domain performance. Prior to conducting these correlations, all variables were assessed for normality using a standardized absolute skew value of 1.96 (Kim, 2013). Pearson’s $r$ correlations were calculated between all normally distributed continuous variables, and Spearman’s $r$ correlations were used for all non-normally distributed variables. Alpha level was set at .05 to determine statistical significance.
CHAPTER IV

RESULTS

Means and standard deviations of all variables used in the study are presented in Table 2. A total of 19 HIV+ participants were included in the sample. Of these, 17 were men (89.5%), and 2 were women (10.5%). The average age of subjects was 55.53 years ($SD = 9.22$) with a range of 30 to 71 years. Ten participants in this sample identified themselves as African-American (52.6%), and nine as Caucasian (47.4%). The mean education level was 14.42 years ($SD = 2.04$), with a range of 10-18 years. Median CD4 count in this study was 584, with an inner quartile range of 412. Median $log_{10}$ viral load level was 4.82, with an inner quartile range of 1.53. Means and standard deviations for all neuropsychological domains are also presented in Table 2.

The average BDI-II total score in this sample was 6.32 ($SD = 5.37$), with scores ranging from 0 to 20. According to empirically established cut-off scores in the BDI-II manual, approximately 89.5% ($n = 17$) of participants scored in the range typically considered as non-depressed (0-13), 5.3% ($n = 1$) in the range considered mildly depressed (14-19), and 5.3% ($n = 1$) in the range labeled moderately depressed (19-26) (Beck, Steer & Brown, 1996). The mean apathy score (BDI-II-MM factor scale) in the current sample was 2.21 ($SD = 1.96$). Scores on this scale ranged from 0-6. The mean score on the Self-Reproach scale was 2.11 ($SD = 2.66$), with scores ranging from 0-9. The average psychosocial impairment (BFIS-LF total impairment score) score in this sample was 17.61 ($SD = 18.36$), with scores ranging from 0 to 71.

Table 2

<table>
<thead>
<tr>
<th>Sample characteristics ($N = 19$)</th>
<th>$M$</th>
<th>$SD$</th>
<th>$Min$</th>
<th>$Max$</th>
<th>$Range$</th>
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25
Demographic variables

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.53</td>
<td>9.22</td>
<td>30</td>
<td>71</td>
<td>41</td>
</tr>
<tr>
<td>Education (years)</td>
<td>14.42</td>
<td>2.04</td>
<td>10</td>
<td>18</td>
<td>8</td>
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</tbody>
</table>

NP domains

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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</thead>
<tbody>
<tr>
<td>Verbal fluency</td>
<td>53.97</td>
<td>9.30</td>
<td>29</td>
<td>70.5</td>
<td>41.5</td>
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<tr>
<td>Executive functioning</td>
<td>50.16</td>
<td>5.68</td>
<td>39</td>
<td>60.00</td>
<td>21</td>
</tr>
<tr>
<td>Processing speed</td>
<td>51.68</td>
<td>7.10</td>
<td>35.33</td>
<td>60.67</td>
<td>25.33</td>
</tr>
<tr>
<td>Attention/working memory</td>
<td>47.21</td>
<td>8.94</td>
<td>33</td>
<td>70</td>
<td>37</td>
</tr>
<tr>
<td>Learning</td>
<td>42.66</td>
<td>11.74</td>
<td>23.5</td>
<td>62</td>
<td>38.5</td>
</tr>
<tr>
<td>Memory</td>
<td>43.84</td>
<td>10.08</td>
<td>29.5</td>
<td>63</td>
<td>33.5</td>
</tr>
<tr>
<td>Motor functioning</td>
<td>51.68</td>
<td>8.12</td>
<td>41</td>
<td>68.5</td>
<td>27.5</td>
</tr>
<tr>
<td>Global functioning</td>
<td>49.06</td>
<td>5.37</td>
<td>34.43</td>
<td>55.5</td>
<td>21.07</td>
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</table>

Psychiatric and functional

BDI-II

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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</thead>
<tbody>
<tr>
<td>Total score</td>
<td>6.32</td>
<td>5.37</td>
<td>0</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mood-Motivation</td>
<td>2.21</td>
<td>1.96</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Self-Reproach</td>
<td>2.11</td>
<td>2.66</td>
<td>0</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>BFIS-LF total impairment</td>
<td>18.58</td>
<td>18.31</td>
<td>0</td>
<td>71</td>
<td>71</td>
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</tbody>
</table>

HIV disease characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mdn (IQR)</th>
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</thead>
<tbody>
<tr>
<td>CD4 cell count</td>
<td>584 (412)</td>
</tr>
<tr>
<td>Log_{10} viral load level</td>
<td>4.82 (1.53)</td>
</tr>
</tbody>
</table>

Hypothesis 1: Relationship Between BDI-II Factors and Neuropsychological Functioning

1) Apathy will be significantly associated with neuropsychological functioning, while depression will not be significantly associated with neuropsychological functioning.
   a. Higher scores on the Mood-Motivation disturbance (MM) scale of the BDI-II will be significantly associated with worse performance on measures of executive functioning and motor functioning.
   b. The Self-Reproach (SR) scale of the BDI-II will not be significantly associated with neuropsychological functioning.
In order to test our first set of hypotheses, bivariate correlations examining BDI-II factor scales and NP domains were computed. Results from this investigation are reported in Table 3. Contrary to the study’s hypotheses, apathy was not significantly associated with neuropsychological functioning in this study. Scores on the Mood-Motivation disturbance scale were not associated with NP performance on measures of verbal fluency \( (r = .30, p > .05) \), executive functioning \( (r = .44, p > .05) \), processing speed \( (r = .09, p > .05) \), attention/working memory \( (r = .01, p > .05) \), learning \( (r = -.03, p > .05) \), memory \( (r = -.07, p > .05) \), motor functioning \( (r = -.10, p > .05) \), or global functioning \( (r = .01, p > .05) \). However, depression, as measured by scores on the BDI-II Self-Reproach scale, significantly correlated with NP performance in learning \( (r = .50, p < .05) \) and attention/working memory \( (r = .53, p < .05) \), such that higher levels of depressive symptoms comprised of negative self-views associated with higher scores on subtests measuring learning and attention/working memory.

Table 3

Bivariate correlations between BDI-II factor scales, neurocognitive domains, and BFIS-LF total impairment score

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mood-Motivation</th>
<th>Self-Reproach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal fluency</td>
<td>.30</td>
<td>.13</td>
</tr>
<tr>
<td>Executive functioning</td>
<td>.44</td>
<td>.16</td>
</tr>
<tr>
<td>Processing speed</td>
<td>.09</td>
<td>.35</td>
</tr>
<tr>
<td>Attention/working memory</td>
<td>.01</td>
<td><strong>.50</strong></td>
</tr>
<tr>
<td>Learning</td>
<td>-.03</td>
<td><strong>.53</strong></td>
</tr>
<tr>
<td>Memory</td>
<td>-.07</td>
<td>.36</td>
</tr>
<tr>
<td>Motor functioning</td>
<td>-.10</td>
<td>-.24</td>
</tr>
<tr>
<td>Global functioning</td>
<td>.01</td>
<td>.36</td>
</tr>
<tr>
<td>BFIS-LF total impairment</td>
<td>.19</td>
<td>.42</td>
</tr>
</tbody>
</table>

\* \( p < .05 \), two-tailed.
Hypothesis 2: Relationship Between BDI-II Factors and Psychosocial Impairment

2) Apathy will be significantly associated with psychosocial impairment while depression will not be significantly associated with psychosocial impairment.

a. Higher scores on the Mood-Motivation disturbance (MM) scale of the BDI-II will be significantly associated with higher BFIS-LF total impairment scores.

b. The Self-reproach (SR) scale of the BDI-II will not be significantly associated with BFIS-LF total impairment score.

To address our second set of hypotheses, bivariate correlations were performed to determine whether apathy and depression associated with psychosocial functioning in this sample. First, we calculated the BFIS-LF total impairment score by summing all 15 items on the BFIS-LF. Correlations were then computed between BDI-II factor scales and total impairment score. Results from these analyses are presented in Table 3. Contrary to our predictions, apathy was not significantly associated with psychosocial impairment in this sample, \( r = .19, p > .05 \). Scores on the Self-Reproach factor scale were also unrelated to functioning disability in this sample, \( r = .42, p > .05 \).

Exploratory Analyses

The results presented above suggest that apathy, as measured by the Mood-Motivation disturbance scale of the BDI-II, is not associated with psychosocial functioning or neuropsychological performance in patients with HIV. Because this is the first study to look at psychosocial functioning in HIV, we wished to further explore the distribution of scores on individual functioning domains in this sample. Table 4 provides means and standard deviations for each BFIS-LF item and the prevalence with which
each item was positively endorsed (i.e., a non-zero or 99 response). Mean ratings ranged from a low of 0 for Item 15 (In taking care of and raising children), to a high of 2.46 for Item 3 (In your work or occupation). The most frequently endorsed items included Item 14 (In maintaining your health), which was endorsed by 79% of participants, and Item 2 (In getting chores completed at home and managing the household), which was endorsed by 53% of participants. Item 1 (In your home life with immediate family), Item 5 (in relationships with friends), Item 9 (In management of your money, bills, and debts), and Item 12 (In your organization and management of daily responsibilities) were all endorsed by 47% of participants.

Table 4

Means, standard deviations, and prevalence of the 15 BFIS-LF items

<table>
<thead>
<tr>
<th>BFIS-LF Major Life Activities</th>
<th>M</th>
<th>SD</th>
<th>% Endorsed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In your home life with immediate family</td>
<td>1.71</td>
<td>2.28</td>
<td>47</td>
</tr>
<tr>
<td>2. In getting chores completed at home and managing your household</td>
<td>1.53</td>
<td>2.07</td>
<td>53</td>
</tr>
<tr>
<td>3. In your work or occupation</td>
<td>2.46</td>
<td>2.67</td>
<td>42</td>
</tr>
<tr>
<td>4. Social interactions with strangers and acquaintances</td>
<td>1.67</td>
<td>2.22</td>
<td>42</td>
</tr>
<tr>
<td>5. In relationships with friends</td>
<td>1.05</td>
<td>1.39</td>
<td>47</td>
</tr>
<tr>
<td>6. In activities in the community (church, clubs, social groups, organizations)</td>
<td>1.19</td>
<td>1.68</td>
<td>37</td>
</tr>
<tr>
<td>7. In any educational activities (college, night classes, technical training, occupational training)</td>
<td>.50</td>
<td>1.07</td>
<td>11</td>
</tr>
<tr>
<td>8. In marital, co-living, or dating relationships</td>
<td>2.00</td>
<td>2.24</td>
<td>42</td>
</tr>
<tr>
<td>9. In management of your money, your bills, and your debts</td>
<td>2.41</td>
<td>2.92</td>
<td>47</td>
</tr>
<tr>
<td>10. In driving a motor vehicle and in your history of citations and accidents</td>
<td>1.31</td>
<td>2.10</td>
<td>26</td>
</tr>
<tr>
<td>11. In your sexual activities and sex relations with others</td>
<td>2.13</td>
<td>2.83</td>
<td>42</td>
</tr>
<tr>
<td>12. In your organization and management of your daily responsibilities</td>
<td>1.33</td>
<td>1.75</td>
<td>47</td>
</tr>
<tr>
<td>13. In caring for yourself daily (dressing, bathing, hygiene, eating, sleeping, etc)</td>
<td>1.11</td>
<td>1.88</td>
<td>37</td>
</tr>
</tbody>
</table>
Because this study was the first to replicate the factor solution model of the BDI on the BDI-II, exploratory analyses were conducted to examine the distribution of scores on individual BDI-II items. Table 5 presents means and standard deviations for each BDI-II item, as well as the prevalence with which each BDI-II item was positively endorsed (i.e., a non-zero response). Average ratings ranged from a low of .11 for Item 1 (Sadness) and Item 9 (Suicidal ideation), to a high of .74 for Item 15 (Decreased initiative/loss of energy). The most frequently endorsed items in the sample included Item 15 (Decreased initiative/loss of energy), which was endorsed by 74% of the sample, Item 16 (Sleep disturbance), which was endorsed by 47% of the sample, Item 3 (Past failure), endorsed by 37% of participants, and Item 4 (Loss of interest), endorsed by 37% of participants.

Table 5
Means, standard deviations, and prevalence of the 21 items on the BDI-II

<table>
<thead>
<tr>
<th>BDI-II item</th>
<th>M</th>
<th>SD</th>
<th>% Endorsed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sadness</td>
<td>.11</td>
<td>.32</td>
<td>11</td>
</tr>
<tr>
<td>2. Pessimism</td>
<td>.26</td>
<td>.45</td>
<td>26</td>
</tr>
<tr>
<td>3. Past failure</td>
<td>.37</td>
<td>.50</td>
<td>37</td>
</tr>
<tr>
<td>4. Loss of pleasure</td>
<td>.37</td>
<td>.50</td>
<td>37</td>
</tr>
<tr>
<td>5. Guilty feelings</td>
<td>.21</td>
<td>.42</td>
<td>21</td>
</tr>
<tr>
<td>6. Punishment feelings</td>
<td>.21</td>
<td>.71</td>
<td>11</td>
</tr>
<tr>
<td>7. Self-dislike</td>
<td>.47</td>
<td>.77</td>
<td>32</td>
</tr>
<tr>
<td>8. Self-criticalness</td>
<td>.26</td>
<td>.56</td>
<td>21</td>
</tr>
<tr>
<td>9. Suicidal ideation</td>
<td>.11</td>
<td>.32</td>
<td>11</td>
</tr>
<tr>
<td>10. Crying</td>
<td>.21</td>
<td>.71</td>
<td>11</td>
</tr>
<tr>
<td>11. Agitation</td>
<td>.11</td>
<td>.32</td>
<td>11</td>
</tr>
<tr>
<td>12. Loss of interest</td>
<td>.26</td>
<td>.45</td>
<td>26</td>
</tr>
<tr>
<td>13. Indecisiveness</td>
<td>.16</td>
<td>.38</td>
<td>16</td>
</tr>
</tbody>
</table>
Because this study is the first to examine the relationship between psychosocial functioning and these specific BDI-II subscales, we wished to further explore the associations between these factors and individual items on the BFIS-LF. Correlations from this investigation are presented in Table 6. Apathy was not significantly associated with psychosocial functioning in these analyses; however, the BDI-II SR scale significantly associated with higher levels of impairment on Item 7 (In any educational activities [e.g. college, night classes, technical training and occupational training]) on the BFIS-LF, $r = .76$, $p < .05$.

Table 6

<table>
<thead>
<tr>
<th>BFIS-LF Major Life Activities</th>
<th>Mood-Motivation</th>
<th>Self-Reproach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In your home life with immediate family</td>
<td>-.01</td>
<td>-.04</td>
</tr>
<tr>
<td>2. In getting chores completed at home and managing your household</td>
<td>.03</td>
<td>.09</td>
</tr>
<tr>
<td>3. In your work or occupation</td>
<td>.13</td>
<td>.37</td>
</tr>
<tr>
<td>4. Social interactions with strangers and acquaintances</td>
<td>.22</td>
<td>.24</td>
</tr>
<tr>
<td>5. In relationships with friends</td>
<td>.02</td>
<td>.20</td>
</tr>
<tr>
<td>6. In activities in the community (church, clubs, social groups, organizations)</td>
<td>.19</td>
<td>.37</td>
</tr>
<tr>
<td>7. In any educational activities (college, night classes, technical training, occupational training)</td>
<td>.40</td>
<td>.76*</td>
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<tr>
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</tr>
<tr>
<td>8. In marital, co-living, or dating relationships</td>
<td>.49</td>
<td>.30</td>
</tr>
<tr>
<td>9. In management of your money, your bills, and your debts</td>
<td>.06</td>
<td>.28</td>
</tr>
<tr>
<td>10. In driving a motor vehicle and in your history of citations and accidents</td>
<td>.14</td>
<td>-.06</td>
</tr>
<tr>
<td>11. In your sexual activities and sex relations with others</td>
<td>-.02</td>
<td>.31</td>
</tr>
<tr>
<td>12. In your organization and management of your daily responsibilities</td>
<td>.24</td>
<td>.29</td>
</tr>
<tr>
<td>13. In caring for yourself daily (dressing, bathing, hygiene, eating, sleeping, etc)</td>
<td>.14</td>
<td>.05</td>
</tr>
<tr>
<td>14. In maintaining your health (exercise, nutrition, preventative medical and dental care, etc.)</td>
<td>.35</td>
<td>.39</td>
</tr>
<tr>
<td>15. In taking care of and raising your children.</td>
<td>.00</td>
<td>.00</td>
</tr>
</tbody>
</table>

* $p < .05$, two-tailed.
CHAPTER V

DISCUSSION

The purpose of the present study was to evaluate the relationship between apathy, depression, cognition and psychosocial functioning in a sample of adults with HIV-infection. To our knowledge, this is the first study to replicate the model proposed by Castellon et al. (2006) using the revised version of the BDI (BDI-II), and to examine the association between these HIV-associated psychiatric disturbances and psychosocial functioning in the context of HIV. Contrary to the study hypotheses, apathy was not associated with neuropsychological functioning in this sample. Moreover, scores on the Mood-Motivation disturbance scale were unrelated to performance on measures of verbal fluency, executive functioning, processing speed, attention/working memory, learning, memory, motor functioning, and global functioning. This evidence contradicts the findings obtained in previous studies (Paul et al., 2005; Castellon et al., 2000, 2006; Kamat et al., 2012). However, a significant, positive association was observed between depression, as measured by the BDI-II SR factor scale, and NP performance on measures of learning and attention/working memory in this sample. In other words, as depressive symptoms involving negative self-views increased, performance scores on measures of learning and attention/working memory also increased. These results are inconsistent with results reported in previous BDI factor analytic studies (Castellon et al., 2006), and previous evidence suggesting that apathy may be a unique marker of CNS disruption in patients with neurologic conditions (Rabkin et al., 2000). Contrary to previous findings, our results suggest that depression, particularly self-reproach, may be a more accurate indicator of neurocognitive changes in HIV+ individuals than apathy (Castellon et al.,
2006). Considering the current study’s operationalization of self-reproach as a generalized negative self-view, this may implicate that symptoms including: feelings of past failure, pessimism regarding the future, self-dislike, self-criticalness, and feelings of guilt and punishment may signify greater HIV-associated CNS involvement among HIV+ individuals than apathy. One alternative explanation for this may be due to the HIV-related stigma. Since the beginning of the HIV/AIDS epidemic, individuals with the disease have reported being subjected to stigmatization and discrimination (Collani, Grumm & Streicher, 2010). Consequently, many individuals internalize these events, and in turn perceive themselves as devalued members of society (Emlet, 2007). With that being said, it is possible that this clinical profile of symptoms may be attributable to these sorts of sociocultural stressors. Nevertheless, these results highlight the importance of considering additional symptoms of depression, particularly feelings of self-reproach, when determining NP performance ability in individuals with HIV.

Contrary to the study’s second set of hypotheses, correlations revealed no significant association between apathy (i.e., BDI-II Mood-Motivation disturbance scale) and psychosocial impairment (i.e., BFIS-LF total impairment score). Depression scores (i.e., BDI-II Self-Reproach factor scale) were also unrelated to psychosocial impairment in this sample. However, exploratory analyses revealed a significant, positive correlation between the BDI-II SR scale and psychosocial impairment on Item 7 (In any educational activities [e.g. college, night classes, technical training and occupational training]) on the BFIS-LF. In other words, as severity of depressive symptoms involving negative cognitions towards the self increased, level of impairment in functioning on activities related to educational advancements in academic/vocational settings also increased. This
finding is consistent with previous literature that has linked depressed mood to poor
functional status to (e.g. instrumental activities of daily living, medication adherence, and
quality of life) in HIV+ patients (Castellon et al., 1998, 2000; Cysique et al., 2007;
Heaton et al., 2004). Given the broad specificity of this item on the BFIS-LF, this may
implicate that impairment in this circumstance may actually serve as an early indicator of
functional decline in this population. Thus, depressed individuals with self-reproach
symptoms may be more susceptible to real-world functioning deficits of this nature than
individuals without these symptoms. As this was the first study to empirically examine
the relationship between psychosocial functioning and these specific dimensions of
depression in HIV, further examination exploring both psychosocial functioning and the
factor solution model of the BDI-II is needed in this patient population. Such information
may elucidate the impact these specific symptoms of depression have on important
psychosocial outcomes in HIV-infected cohorts.

Exploratory analyses were conducted to examine the distribution of scores on
individual items on the BDI-II and BFIS-LF in this sample. The most frequently endorsed
item on the BDI-II was Item 15 (Decreased initiative/loss of energy), which was endorsed
by 74% of the sample. To be noted, this item most strongly captured the construct of
apathy in Castellon et al.’s (2006) factor solution model, and other prior factor analytic
studies, and is consistent with recent research showing symptoms of apathy to be largely
prevalent in HIV-infected cohorts (Castellon et al., 1998, 2000, 2006; Rabkin et al., 2000,
Startup et al., 1992; Steer et al., 1987). Although apathy ratings (total BDI-II scores on
the Mood-Motivation scale) were unrelated to NP and psychosocial functioning in this
sample, this data suggests that this syndrome can still be considered a neuropsychiatric
correlate of HIV-infection. Thus, further study is needed in this field to better understand the specific cognitive and functional mechanisms of apathy in patients with HIV.

**Limitations and Directions for Future Research**

Although this study contributes to the understanding of HIV-associated psychiatric disturbances in persons with HIV, certain limitations exist. First, this study is limited by its relatively small sample size. Thus, some of the non-significant correlations reported in this study may be attributable to low statistical power. For this reason, these findings cannot be generalized to the broader HIV community based on this study alone. Another limitation in the study is the use of self-report questionnaires to measure BDI-II factor scales and psychosocial functioning. Although the BDI-II and BFIS-LF have strong psychometric properties, there is an inherent risk of self-report biases to confound the data. For example, participants’ desire to be viewed positively may result in decreased reporting of depression and functioning impairment. To improve the reliability of these results, future research should include the addition of multiple self-report measures as well as objective measures of apathy, depression and functioning such as laboratory-based functional measures and/or previous diagnostic history. Such information may aide in the development of appropriate diagnostic tools to help identify individuals at particular risk for cognitive and functional impairments of this nature.

Another limitation of the study is the relatively limited range of scores on the BDI-II and BFIS-LF. In general, approximately 89.5% (n = 17) of the sample scored in the range typically considered non-depressed (BDI-II total scores between 0 and 13), and 11% (n = 2) scored in the mild to moderate range of depression (BDI-II total scores between 14 and 26). The average total impairment score on the BFIS-LF in this sample
was 17.61 ($SD = 18.36$), indicating overall low levels of impairment in psychosocial functioning. These low prevalence rates make for a very challenging prediction problem, whereas in populations having higher base rates of depression and functioning impairments would significantly increase the predictive value of these results. Future study should examine populations with more severely depressed and impaired subjects to get a more accurate depiction of the neuropsychological and functional consequences of these HIV-associated psychiatric syndromes.

Lastly, participants in this sample were relatively healthy and did not have significantly advanced HIV disease. Only 1 participant had CD4 T-cell count less than 200 (i.e., required for an AIDS diagnosis), and the median CD4 count was 584. This likely limited our ability to detect a relationship between apathy (as an indicator of HIV-related neurological damage) and neuropsychological and psychosocial outcomes. Future studies should explore these constructs in less healthy individuals with more severe HIV disease progression. Such information would be useful in the development of accurate prognostic tools that can be utilized in clinical settings to screen for depressive symptoms associated with specific deficits in functioning in patients with HIV.

**Summary**

Although the associations reported in this study were unsupportive of the study’s main hypotheses that apathy uniquely contributes to cognition and psychosocial functioning outcomes in patients with HIV, these correlations showed depression (as measured by the BDI-II SR factor) to be significantly associated with neurocognitive performance in learning and attention/working memory. Additionally, exploratory correlations showed depression to be associated with higher levels of impairment in
activities involving functioning in advanced educational and vocational settings. These findings reinforce the potential real world and cognitive correlates of depression in adults with HIV, and iterate the importance of accurately detecting this condition in this population. As survival rates in patients with HIV have dramatically increased, future research on the neurocognitive and functional consequences of psychiatric disturbances associated with HIV is critical. Further exploration in this field will hopefully promote the development and implementation of efficacious screening tools that can be used to treat these psychiatric conditions and assist in the diagnosis of HIV-associated neurocognitive disorders (HAND) in the comprehensive care of HIV infected individuals.
REFERENCES


cerebral volume loss in human immunodeficiency virus infection. *Archives of Neurology, 50*(3), 250–255.


