The relationship of apathy to executive functioning among HIV-positive adults

Sloane Kimberly Miller

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THE RELATIONSHIP OF APATHY TO EXECUTIVE FUNCTIONING AMONG
HIV-POSITIVE ADULTS

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

by

Sloane Kimberly Miller

May, 2012

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This clinical dissertation, written by

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DOCTOR OF PSYCHOLOGY

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ACKNOWLEDGEMENTS

I would not have been able to complete my dissertation without the guidance of my committee members and support from my friends and family. The members of my dissertation committee have generously given their time and expertise to better my work. I would like to express my sincere gratitude to my dissertation chair, Dr. Mitchell, for his exceptional guidance, patience and providing me with consistent and thoughtful feedback. I would like to thank my committee member, Dr. Himelstein, who helped fuel my passion for neuropsychological assessment at the start of graduate school and has since been instrumental in supporting my academic pursuits. I would also like to thank Dr. Castellon, whose prior research of neuropsychological functioning within HIV positive populations inspired my current research. As a friend and colleague Dr. Castellon was always willing to provide guidance along with much appreciated comedic relief. Many thanks to Dr. Hinkin for providing me with invaluable research and clinical opportunities over the years and for facilitating my research by sharing his esteemed database. I would like to give a special thank you to my mentors Dr. Kravitz and Dr. Warner for their invaluable supervision, teachings and personal guidance over the years. I would also like to thank my current internship supervisor Dr. Gordon as well as my fellow interns at NYU Rusk Institute of Rehabilitation Medicine for their support and encouraging words throughout this final stretch. I am grateful to be working with such intelligent, thoughtful, and hard-working colleagues within the field of neuropsychology. Lastly, I would like to thank my parents, four elder sisters, and elder brother, as well as my dear friend’s Marissa Pipkin, Shereen Kianmahd, and Jill Norman for their emotional support and for always encouraging me with their best wishes and reassuring words.
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ABSTRACT

As the HIV population ages and HAART extends the life span of older HIV+ individuals, it is important to address the neuropsychological, cognitive, and emotional manifestations of HIV in this sub-population. The purpose of the present study was to examine whether apathy and depressive symptoms were associated with executive functioning in older HIV+ individuals. This archival study explored whether four items from the Beck Depression Inventory, Second Edition (BDI-II) could serve as an index of apathy and whether higher scores on these items would be related to greater impairment on measures of executive functioning. The sample consisted of 95 older HIV+ persons who completed neurocognitive tests of executive functioning as well as the BDI-II as part of a larger study examining the relationship between HIV and aging. The measures of executive functioning were: the Stroop Color Word Interference Test; the Trail Making Test, Part B; the Controlled Word Association Test; and the Wisconsin Card Sorting Test-64. Four items from the BDI-II - reflecting loss of pleasure, loss of interest, loss of interest in sex, and difficulty making decisions - were selected on the basis of prior research and rational analysis as likely to represent apathy. Cronbach’s alpha reliability analysis determined that these four items of the BDI-II clustered together with acceptably high internal consistency in the present sample (.75). However, overall scores on the BDI-II, including on the four items thought to reflect apathy, tended to be surprisingly low, indicating little self-reported depressive symptomatology. Consistent with prior research, the overall BDI-II showed impressive internal consistency reliability in the present sample (.92). It was predicted that higher apathy scores would be associated with poorer performance on measures of executive functioning. The sample was ethnically
diverse, predominantly male, and had a mean age of 55.26 years. The mean years of education was 13.67, while the mean estimated level of premorbid intellectual functioning was 97.73. The results showed there was no significant relationship between the hypothesized apathy items and executive functioning performance. Moreover, findings showed no relationship between overall BDI-II scores and performance on measures of executive functioning. The limitations of this archival study included the absence of an independent criterion measure for the construct of apathy. Other findings, additional limitations, and suggestions for future research are discussed.
Introduction

Background

The Centers for Disease Control and Prevention (CDC, 2008) estimate that over 1 million individuals in the United States are infected with the human immunodeficiency virus (HIV). Since the introduction of highly active antiretroviral therapy (HAART), survival rates associated with HIV have improved dramatically (de Olalla et al., 2002; Murphy et al., 2001). However, despite advances in the diagnosis and treatment of HIV infection, most antiviral treatments do not cross the blood-brain barrier (Gartner & Liu, 2002; Gartner, 2000), leaving the CNS vulnerable to the damaging neurotropic effects of HIV (Ellis, Langford, & Masliah, 2007). With the introduction of HAART, there has been a greater life expectancy for HIV infected persons, which has ultimately resulted in a growing population of older HIV+ individuals. Progress in treatment has transformed HIV from an untreatable illness with a dire prognosis to a more chronic illness with complex cognitive and neuropsychiatric manifestations (Bornstein et al., 1993a; Gorman, Foley, Ettenhofer, Hinkin, & van Gorp, 2009; McCombe, Noorbakhsh, Buchholz, Trew, & Power, 2009; Starace et al., 2002).

Neuropsychological Factors Associated With HIV

Cognitive impairment has been found to occur in 55% to 65% of people with AIDS and it has been estimated that between 30% and 50% of HIV+ individuals would experience some form of neurocognitive decline (Heaton et al., 1995). Despite treatment advances in the post-HAART era and reduced frequency of dementia, milder forms of cognitive impairment remain frequent (Antinori et al., 2007; Heaton et al., 2010). HIV infection most prominently affects the cognitive domains of motor functioning, attention,
processing speed, executive functioning, and memory (Ances & Ellis, 2007; Foley, Ettenhofer, Wright, & Hinkin, 2008; Heaton et al., 1995; Woods, Moore, Weber, & Grant, 2009). HIV-related neurocognitive impairment can range from subtle deficits to marked dementia syndromes that disrupt an individual’s daily functioning, employment, and ability to manage important tasks such as managing finances and adhering to medications (Foley et al., 2008; Gorman et al., 2009; Grant, Heaton, & Atkinson, 1995; Heaton & The HNRC Group, 2004; Hinkin, van Gorp, & Satz, 1995). Although the specific mechanisms and effects of HIV infiltration of the CNS are not fully understood, there is research indicating that the frontal-subcortical circuitry is a primary target (Everall, Luthert, & Lantos, 1991; Heaton et al., 1995; von Giesen, Baecker, Heftet, & Arendt, 2001). A recent study from Dawes and colleagues (2008) has shown that executive function impairment is a central characteristic of most HIV neurocognitive impairment profiles. Executive functions include abstraction, problem solving, set shifting and reasoning. Because executive functions are dependent on the frontal cortex, it makes sense that HIV has been found to be associated with executive function impairment (Reger, Welsh, Razani, Martin, & Boone, 2002). Executive dysfunction has been found to be associated with functional deficits that include decreased medication adherence and poorer performance of activities of daily living (Schillerstrom, Horton, & Royall, 2005).

Neuropsychiatric and Neurocognitive Disorder in Older HIV+ Adults

Currently, more than 15% of all US AIDS patients are older than 50 years (CDC, 2007). With the introduction of more effective treatments, mortality rates have dropped and HIV has consequently evolved into a disease that is increasingly affecting older
adults (Valcour et al., 2004). Research findings have supported the hypothesis that older HIV-infected individuals may be at greater risk for cognitive impairment due to the co-occurrence of both older age and HIV disease (Becker, Lopez, Dew, & Aizenstein, 2004; Valcour et al., 2004). Given that HIV infection and normal aging processes are risk factors for neuropsychological compromise, it is not surprising that the older HIV population is particularly vulnerable to neuropsychological impairment. Research suggests that the clinical manifestations of infection among older HIV+ individuals are considerably different than those observed in younger cohorts, because of the increased risk factors and vulnerability for developing cognitive decline (Foley et al., 2008; Valcour et al., 2004). It has also been suggested that neuropsychological deficits are more pronounced in the later stages of HIV infection (Heaton et al., 1995). Therefore, neuropsychological tests may be important tools for detecting deficits present in an older HIV population, especially given that older individuals are more likely than younger persons to exhibit cognitive decline. As the HIV population ages and HAART extends the life span of older HIV+ individuals, it is important to address the neuropsychological and cognitive manifestations of HIV in this sub-population. The purpose of the present study was to examine whether the construct of apathy was associated with executive dysfunction in a sample of older HIV+ individuals. To the extent that a relationship could be identified, it was reasoned that apathy may represent a significant neuropsychiatric indicator of CNS pathology among older HIV+ individuals.

**HIV and Depression**

Depression is common in individuals with a variety of medical illnesses, and appears to be more common among HIV+ individuals than the general population (Basu,
Chwastiak, & Bruce, 2005; Chandra, Desai & Ranjan, 2005; Treisman, Fishman, Schwartz, Hutton, & Lyketsos, 1998). In the U.S., estimated prevalence of depression is 2-10 times higher in people living with HIV/AIDS compared to the general population (Bing et al., 2001; Pence, 2009). Bing and colleagues (2001) showed that as many as 37% of HIV-infected individuals suffered from major depression. Despite medical treatment advances, it remains unclear what factors are contributing to the high prevalence of depression among those with HIV. While researchers have accumulated considerable findings regarding the cognitive consequences of HIV infection, less is known about the neuropsychiatric changes that often surface. The degree to which mood disturbance may manifest differently in primary psychiatric versus primary neurologic populations has been under-studied. The extent to which psychiatric features that accompany HIV, such as depression, anxiety, irritability, and apathy, are a result of insults to the CNS or secondary to medical, social, and financial stressors remains unclear (Castellon, Hinkin, & Myers, 2000; Castellon, Hinkin, Wood, & Yarema, 1998; Rabkin et al., 2000). It has been suggested that the depression associated with HIV is either idiopathic or induced by the illness through direct or indirect pathways. Idiopathic depression stems from factors that cause depression in non-medically ill populations, such as family history of affective disorders, trauma, or adverse life stressors. HIV-provoked depression implies that the mood disorder is either associated with the CNS infiltration of HIV or a response to increased stressors associated with HIV. Treisman et al. (1998) suggest that depression may be the result of neurotropic effects of the virus on the subcortical brain areas that remain vulnerable with HAART treatment. However, most research has found that among HIV+ individuals, depression and anxiety appear to
be less related to the neurotropic effects of the disease (Bornstein et al., 1993b; Carter, Rourke, Murji, Shore, & Rourke, 2003; Castellon et al., 1998; Cole et al., 2007; Heaton et al., 1995; Judd et al., 2005; Rabkin et al., 2000) and more likely stemming from secondary factors such as social stigmatization, marginalization, unemployment, bereavement, compromised social support, and increased medical, legal and financial stressors (Castellon et al., 2000; Grassi et al., 1999; Perez et al., 2005; Roberts, Ciesla, Direnfeld, & Hewitt, 2001). In addition, it is likely that depression is higher among HIV+ individuals because it is idiopathic and comorbid with the risk factors that lead to HIV infection, such as substance abuse and risky sexual behaviors (Bing et al., 2001; Dausey & Desai, 2003). In other words, depression may be a risk factor for contracting HIV and therefore precede actual infection. Gorman and colleagues (2009) suggest that a bidirectional relationship may exist whereby symptoms of idiopathic depression precipitate secondary factors such as poor psychosocial, medical and financial adjustment in individuals with HIV. Overall, a majority of the research postulates that depression is generally not caused by biological factors associated with HIV infiltration, but is rather idiopathic and/or a psychological response to the cognitive deficits and social stressors secondary to HIV.

**HIV and Apathy**

Apathy refers to a state of indifference and a reduction in self-initiated or goal directed thoughts and behaviors; it is frequently seen in CNS disorders that disrupt frontal-subcortical connections (Marin, 1991; van Reekum, Stuss & Ostrander, 2005). Specifically, apathy includes decreased work motivation, decreased social involvement, anhedonia, difficulty making decisions, and anergia. Apathy has been more commonly
reported in patients infected with HIV than in the general population (Castellon et al., 2000; Hinkin, Castellon, Atkinson & Goodkin, 2001; Rabkin et al., 2000). Because patients with depression often have symptoms of apathy, it is difficult to distinguish apathy as a distinct syndrome or merely a symptom of depression (Levy et al., 1998). Nevertheless, apathy has been demonstrated to be qualitatively distinct from depression in HIV+ individuals (Castellon et al., 2006; 1998; Levy et al., 1998). Research conducted with the HIV population has found symptoms of apathy rather than depression to correlate strongly with cognitive dysfunction (Castellon et al., 2006; Cole et al., 2007). In other words, apathy, unlike depression, may reflect a direct consequence of the HIV infection on the brain structures that regulate emotional reactivity. It can be assumed that damage to the frontal area due to HIV infiltration has the potential to produce an apathetic state because this is the area of the brain involved in emotional experiences such as energy, enthusiasm, productivity, and initiative (Cummings, 1993; Levy et al., 1998; Zamboni, Huey, Krueger, Nichelli, & Grafman, 2008). Frontal lobe symptoms such as apathy have been attributed to disruption in subcortical circuits involving the basal ganglia and the frontal lobes (Landes, Sperry, Strauss, & Geldmacher, 2001). Therefore, manifestation of simultaneous apathy and cognitive deficits could be related to the underlying damage of subcortical and frontal systems.

The relationship of apathy to neurocognitive function has been extensively studied in a range of brain disorders (van Reekum et al., 2005). Research has shown apathy to be separate from depression and associated with neurocognitive impairment and neurological pathology seen in stroke, dementia, and Parkinson’s Disease populations (Brodaty et al., 2005; Engelborghs et al., 2006; Kuzis, Sabe, Tiberti,
Dorrego, & Starkstein, 1999; Levy et al., 1998; Oguru, Tachibana, Toda, Okuda, & Oka, 2010; Pluck & Brown, 2002). Among these brain disorders, there are a number of studies finding a consistent relationship between high levels of apathy and poor performance on tests representing executive function (Andersson & Bergedalen, 2002; McPherson, Fairbanks, Tiken, Cummings, & Back-Madruga, 2002; Zgaljardic et al., 2007). There is also research showing a relationship between apathy and executive functioning in populations with psychosis (Faerden et al., 2009). In the Alzheimer’s Disease (AD) population, apathy is a common neuropsychiatric symptom and one of the primary neuropsychiatric manifestations of frontal system dysfunction (Boyle & Malloy, 2004). Cole and colleagues (2007) postulate that because AD and HIV populations have similarly elevated rates of apathy and irritability symptomatology, it further supports the theory that frontal system involvement is underlying the psychiatric manifestations in both populations.

Research focusing on HIV populations suggests that apathy prominence among HIV+ individuals may signify disease associated CNS insult. In the HIV population, disturbance of motivation and goal-directed behavior has been found to correlate with lower neurocognitive performance (Andersson & Bergedalen, 2002; Castellon et al., 1998, 2000, 2006; Cole et al., 2007; Paul et al., 2005a). Castellon et al. (2006) found prominent symptoms of apathy and irritability to be highly related to poorer performance on neuropsychological tasks most dependent upon executive functioning. Paul and colleagues (2005a) similarly found that higher levels of apathy correlated with poor frontal systems functioning such as cognitive flexibility. Neuro-imaging research has provided further preliminary evidence that apathy reflects direct involvement of the CNS
in patients with HIV (Hoare et al., 2010; Paul et al., 2005b). Paul and colleagues (2005b) found that increased ratings of apathy were significantly correlated with lower volume of the nucleus accumbens, a subcortical brain structure that regulates initiation of behavioral activation. All together these findings suggest that symptoms of apathy are likely attributable to the primary CNS effects of the HIV virus on frontal-subcortical circuits. Despite significant research on apathy and neurocognitive functioning in brain disorders, there is a lack of research in this area focusing on the HIV population and even less research focusing on older HIV+ individuals. If apathy is a potential indicator of CNS pathology in medical illness, it is important to assess its presence and its correlates in aging HIV individuals.

**Beck Depression Inventory II**

The current study focused on the “apathy” items of the second revised version of the Beck Depression Inventory (BDI-II; Beck et al., 1996). The BDI-II was developed for the assessment of depressive symptoms that correspond to the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV; APA, 1994) criteria for major depressive disorder. Although the BDI-II is meant to measure the global construct of depression, the question as to whether meaningful groups of items in the questionnaire can be discerned through factor analysis has been of ongoing interest (Beck et al., 1996). Studying the factors that underlie the depression construct is important because recent research indicates that sub-dimensions of depression have different correlates (Vanheule, Desmet, Groenvynck, Rosseel, & Fontaine, 2008).

Castellon and colleagues (2006) conducted a factor analysis of the BDI on a large sample of HIV-infected individuals and found that certain items of the depression rating
scale consistently clustered together to form meaningful factors. Specifically, they found three factors that were labeled Mood-Motivation Disturbance, Self-Reproach, and Somatic Disturbance. Interestingly, these factors were found to be differentially associated with cognitive function in their HIV/AIDS sample. The Self-Reproach factor contained items representing negative cognitions. The Mood-Motivation Disturbance factor contained items related to apathy, sad mood and irritability. The Somatic Disturbance factor contained items related to somatic complaints. Specifically they found that the Mood-Motivation Disturbance factor, which consisted of 7 items reflecting symptoms of apathy, sad mood, and irritability, was the factor most strongly associated with neurocognitive performance. In addition, they found that the neurocognitive domains most closely associated with the Mood-Motivation Disturbance factor were verbal memory, executive functioning, and motor performance. The findings indicate that the apathy, irritability, and sad mood items from the BDI may be more indicative of CNS dysfunction than other items. It was found that disturbance in mood and motivation, more so than negative self-view or somatic disturbance, was related to neurocognitive deficits.

The current study focused specifically on items within the BDI-II that were believed to reflect symptoms of apathy. Items of interest in the current study were comparable to only the apathy items belonging to the Mood-Motivation Disturbance factor found in the Castellon 2006 study and found to load together in prior research on the BDI (e.g. Startup, Rees & Barkham, 1992; Steer, Beck, Riskind, & Brown, 1987; Tanaka & Huba, 1984). The BDI apathy related items found to load together in prior research included (a) decreased work initiative, (b) decreased social initiative, (c)
anhedonia, (d) difficulty making decisions, and (e) anergia. In the current study, symptoms of sad mood and irritability were not evaluated because the researcher was specifically evaluating the apathy component of depression. Even though the current study examined the BDI-II rather than the original BDI, those items reflecting symptoms of apathy have generally remained unchanged in the revised scale. The BDI was merely modified to better complement the DSM-IV criteria for major depressive disorder (Beck, Steer, Ball, & Ranieri, 1996). Items of the BDI-II reflective of apathy symptoms include (a) Loss of pleasure (item 4); (b) Loss of interest (item 12); (c) Difficulty making decisions (item 13); and (d) Loss of energy (item 15). The BDI-II item of Loss of Interest replaced the BDI items relating to social withdrawal to emphasize withdrawal from both interpersonal relationships and activities. In addition, the BDI-II item of Loss of Pleasure replaced the BDI items related to loss of satisfaction and anhedonia. The item related to difficulty making decisions remained unchanged.

Recent research has indicated that it is important to consider overlapping symptoms of HIV disease and somatic symptoms of depression that can inflate scores on depression inventory instruments (Kalichman, Rompa, & Cage, 2000). Kalichman and colleagues (2000) found that removing somatic depression symptoms improved the clinical utility of the BDI in an HIV+ sample. Their findings suggest that clinicians should be cautious regarding somatic symptoms when evaluating depression scores in people living with HIV infection. It has been suggested that somatic symptoms included in most depression measures might be indicators of physical illness, and therefore, diagnostically ambiguous (Castellon et al., 1998). Castellon and colleagues (1998) argued that unlike the somatic symptomatology of depression, the affective/cognitive
symptomatology of depression is a more accurate indicator of mood disturbance among medically ill individuals. Therefore, in the current study, somatic symptoms overlapping with medical illness symptoms, such as fatigue and loss of energy, were not evaluated within the context of apathy because they were considered to be diagnostically ambiguous in a medically ill population. Specifically, the BDI-II items of Loss of Energy and Fatigue were not evaluated in terms of apathy. However, these items were included in our evaluation of overall depression, because somatic symptoms are a significant component of depression.

Overall, prior research has shown that while apathy and depression are overlapping dimensions, they can nevertheless be distinguished from one another and can differentially influence cognitive functioning (Castellon et al., 2006, 1998). However, among HIV patients, it remains unclear whether the symptoms of apathy within depression reflect a direct effect of the virus on subcortical brain circuits or reflect more of a secondary neuropsychiatric manifestation.

**Purpose of the Study**

Many studies have failed to find a consistent relationship between mood and neurocognitive performance among HIV+ individuals (e.g., Bornstein et al., 1993b; Hinkin et al., 1992; von Giesen et al., 2001). However, most studies to date have focused on depression rather than more specific and differentiated components of depression such as apathy. In addition, those few studies that have focused on apathy in HIV populations have studied relatively young persons. Prior research has yet to focus on the relationship between apathy and cognition in a sample of older HIV+ individuals. The aim of the current study was to expand on the prior research on apathy in HIV populations and
improve our understanding of apathy in relation to executive functioning in older HIV+ individuals. This study explored the concept of mood disturbance in HIV populations by breaking down a traditional measure of depression (BDI-II) and examining the items believed to be reflective of apathy, including their relationship to executive functioning. To the researcher’s knowledge, no prior research existed that utilized the BDI-II to explore apathy symptomatology and its relationship to cognitive functioning in an older HIV+ population or any other population. This study aimed to determine whether specific BDI-II items representing symptoms of apathy could be clustered into a component of depression analogous to apathy and whether executive functioning performance would differ between those scoring high and low on this cluster.

The following research questions and hypotheses were addressed. First, to what extent do the apathy items of the BDI-II group together in a sample of older HIV+ individuals? It was hypothesized that the BDI-II apathy items would cluster together with an internal consistency of .70 or higher. Next, how do the BDI-II apathy items relate to executive functioning performance in older HIV+ individuals? It was hypothesized that persons scoring high on the apathy items would perform more poorly on executive function tasks than persons scoring low on the apathy items. In other words, it was predicted that scores on the BDI-II apathy cluster would be inversely related to executive functioning performance. The third research question was as follows: what is the relationship of BDI-II total scores to executive functioning performance in older HIV+ individuals? It was expected that overall BDI-II scores would have an inverse relationship to executive functioning, but the association was expected to be weaker than that shown with the four BDI-II apathy items.
Method

Design

This study was a secondary analysis of primary data gathered from an ongoing longitudinal, case-control study aiming to determine the effect of age on neuropsychological performance in HIV+ persons. The nature of the design was essentially correlational in that the researcher examined the extent to which one factor, i.e., the apathy items on the BDI-II, corresponded to aspects of executive functioning in a sample of older HIV+ persons.

Participants

Subjects for this study were recruited from the West Los Angeles Veterans Administration Medical Center and other community agencies and medical centers in the Los Angeles area specializing in serving HIV-infected individuals. Patients were eligible for the parent study if they were between the ages of 18-40 years or 50 years and older. In addition, participants had to document presence or absence of HIV infection (depending on their group assignment) and had to be proficient in English. Any participants showing evidence of opportunistic infection or central nervous system (CNS) infection other than HIV were excluded. In addition, participants were excluded if they had a history of traumatic brain injury with loss of consciousness greater than 30 minutes, a current diagnosis of seizure disorder, or a current psychotic spectrum disorder (e.g., schizophrenia, bipolar disorder). Patients meeting inclusion criteria were scheduled for an initial visit. All subjects were tested as outpatients. Approval to conduct the original study was granted by the University of California, Los Angeles and the Veteran’s Administration Institutional Review Boards.
Additional exclusion criteria were utilized for the present study. Subjects were excluded if they were under the age of 50. Subjects were also excluded if they presented with medical co-morbidities unrelated to HIV, which may increase risk for cognitive impairment (e.g., brain anoxia, stroke). In addition, we excluded participants who tested positive for cocaine or amphetamines on their initial visit urine screen and simultaneously met criteria for drug dependence over the last 30 days according to self-report. These exclusion criteria were utilized to ensure a clean sample of older HIV+ individuals. In other words, the researcher was attempting to control for factors other than apathy that could account for variance in cognitive performance. The researcher was aware that this would impact generalizability, given that HIV+ individuals often possess a number of the comorbid conditions listed in our exclusion criteria. However, the aim of this study was to determine whether apathy, in the absence of other influential factors, could be found to be associated with deficits in executive functioning. Given the assumption of a medium effect size, a sample size of 64 total was determined to be sufficient to detect the presence of significant differences at an alpha level of 0.05 (Cohen, 1992).

**Neurocognitive Measures**

In the current study, four instruments were used to measure executive functioning. The Stroop Color Word Interference Test (Stroop, 1935) assesses multiple functions including color-naming and word-reading speed, sustained attention, and, in the interference condition, selective attention and the ability to inhibit a habitual response in favor of a more over learned response. It is an overall measure of selective attention and cognitive flexibility. The current study utilized the Golden version of this test (Golden, 1978). In the color-word interference condition the subject reads the color in which color
names are printed and disregards their verbal content. The dependent variable of interest is the number of trials completed in 45 seconds for this color-word interference condition. High test-retest reliability coefficients have been reported for the Golden version of the Stroop (Connor, Franzen, & Sharp, 1988; Franzen, Tishelman, Sharp, & Friedman, 1987). In addition, it has been found that the interference score correlates moderately well with other measures of attention (MacLeod & Prior, 1996; Weinstein, Silverstein, Nader, & Turnbull, 1999) and neuroimaging studies have shown that the frontal lobe is the most consistent region of activation during this test (Brown et al., 1999; Mead et al., 2002).

The Trail Making Test (Reitan, 1958) is a brief test of visual-motor function, attention, and psychomotor speed. Part B of this task requires switching conceptual set (alternating between connecting numbers and letters in ascending sequence) and measures number-letter switching ability. This test has been shown to be a valid measure of cognitive impairment (Bradford, 1992; Gaudino, Geisler & Squires, 1995) and to have high interrater reliability (Fals-Stewart, 1992). For this particular study, only Part B performance was examined and the dependent variable of interest was the completion time in seconds for Part B. This test indicates one’s ability to execute and modify a plan of action, and has been found to be sensitive to frontal lobe damage (Boll, 1981; Lezak, Howieson & Loring, 2004). Studies have found that cognitive flexibility, also referred to as “attentional set-shifting,” could capture executive abilities underlying Part B performance (Chaytor, Schmitter-Edgecombe, & Burr, 2006; Kortte, Horner, & Windham, 2002).
The Controlled Oral Word Association Test (Benton, Hamsher, Varney & Spreen, 1983) assesses semantic and phonemic verbal fluency. Over the course of three, one-minute trials, the subject must name as many words as he or she can starting with a given letter (“F”, “A”, and “S”) and, in the final one-minute trial, he or she must name as many types of animals as possible. This test has been shown to have high test-retest reliability (Levine, Miller, Becker, Selnes, & Cohen, 2004), high interrater reliability (Ross, 2003) and good validity (Troyer, 2000). In the current study, only phonemic (FAS) performance was examined and the dependent variable of interest was the total number of words generated. The verbal fluency test has been described as an executive function test (Lezak et al., 2004). Moreover, research has shown that patients with frontal damage produced significantly fewer responses on verbal fluency tests compared with patients with lesions in other brain areas (Perret, 1974).

The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948) is widely regarded as a valid test of frontal lobe functioning (Robinson, Heaton, Lehman, & Stilson, 1980; Lezak et al., 2004) with generally strong test-retest reliability (Tate, Perdices, & Maggiotto, 1998). The WCST assesses abstract reasoning, problem solving and the ability to adapt cognitive strategies to external changing feedback (Chelune & Baer, 1986). The dependent variable of interest in the current study was the number of perseverative errors on the WCST-64 computer version of this test - an abbreviated form of the standard 128-card version of the WCST (Kongs, Thompson, Iverson, & Heaton, 2000). A perseverative error refers to the number of errors in which the participant perseverates on a prior matching strategy, reflecting failure to shift to the new sorting criterion. Among the various scoring norms of the WCST, perseverative errors are
regarded as the main signs of frontal dysfunction (Greve, Stickle, Love, Bianchini, & Stanford, 2005).

**Neuropsychiatric Measure**

The Beck Depression Inventory, 2nd Edition (BDI-II; Beck et al., 1996), a 21-item self-report rating scale containing questions pertaining to the presence and intensity of various cognitive, affective, and somatic symptoms of depression over a two-week period, was administered to all participants. Each item is a list of four statements arranged in increasing severity about a particular symptom of depression. There is a four-point scale for each item ranging from 0 (symptom absent) to 3 (presence of symptom is pronounced). Each of the 21 items is summed to give a single score for the BDI-II. Cut score guidelines for the BDI-II are as follows: Total score of 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 is severe. The timeframe and items are aligned with depression criteria of the DSM-IV. The test requires a 5th to 6th grade reading level (Groth-Marnat, 2009) and is intended for persons 13 years of age and older. According to test authors, the BDI-II demonstrated internal consistency reliability of .92 in a sample of 500 psychiatric patients, and test-retest reliability (one week interval) of .93 in a small sample of outpatients (Beck et al., 1996). Evaluations of the content, concurrent, and discriminant validity of the BDI-II have been impressive, and over 1,000 research studies have employed a version of the Beck Depression Inventory (Groth-Marnat, 2009).

Research has indicated that the BDI-II is a reliable and valid measure of depression for use in outpatient medical populations, including among ethnically and socioeconomically diverse communities (e.g., Jarjoura et al., 2004; Joe, Woolley, Brown,
Ghahramanlou-Holloway, & Beck, 2008; Groth-Marnat, 2009; Grothe et al., 2005). It has also been used with diverse samples of HIV+ individuals (e.g., Weiser et al., 2006) and has been found to be a sufficiently reliable and valid measure for assessing depression in an HIV positive sample (Lipps et al., 2010). Therefore, the BDI-II was determined be an appropriate measure of depressive symptoms in the present sample.

The apathy variable of interest in the current study consisted of the following items of the BDI-II: (a) Loss of Pleasure (item 4); (b) Loss of Interest (item 12); (c) Indecisiveness (item 13); and (d) Loss of Interest in Sex (item 21). To the researcher’s knowledge, there had been no published research attempts to examine the apathy items of the BDI-II prior to the current study. Therefore, the current study aimed to look specifically at items that were comparable to those items previously found to load together in the original BDI and to be reflective of disturbance in motivation (Castellon et al., 2006; Startup et al., 1992; Steer et al., 1987; Tanaka & Huba, 1984). Five of the seven original BDI items in the Mood-Motivation Disturbance factor identified by Castellon and colleagues (2006) appeared reflective of apathy. Those items addressed included decreased work initiative, decreased social initiative, anhedonia, difficulty making decisions, and anergia. Those items appeared similar to items found on established apathy scales (e.g., The Apathy Evaluation Scale-Self Report Version; Marin, 1991). In the current study, somatic symptoms overlapping with medical illness symptoms, such as fatigue and loss of energy, were not evaluated within the context of apathy because they were considered to be diagnostically ambiguous in a medically ill population. Items of interest were cognitive-affective and directly correspond to the “apathy” items found in previous research on the BDI. Therefore, items reflective of the
anergia item from the earlier BDI research were not included among the apathy-related BDI-II items selected for study in the present investigation. Loss of Interest in Sex was included in the present “apathy” construct because it inquires about interest in sexual activity rather than changes in sexual activity.

Procedures

All participants completed a comprehensive neuropsychological test battery between the years of 2005 and 2010 at the West Los Angeles Veterans Administration Medical Center. The battery was administered by trained psychometrists who were supervised by a board certified neuropsychologist. The neuropsychological evaluation was extensive and included multiple performance measures of several cognitive domains. Participants’ sociodemographic data, HIV status and health information (e.g., viral load, CD4 count, medications, duration of illness, and health conditions) were obtained once informed consent had been established. Participants completed all screens, questionnaires, and neuropsychological tests within a one-day period. Initial visit duration was typically 6-7 hours and participants were financially compensated $90.00 at the end of the day.

The current study examined a sub-sample of Visit 1 data that included neurocognitive test results, specifically in the domain of executive functioning, as well as BDI-II scores, and demographic information. The current study only examined the older age group (older ≥ 50 years). Neurocognitive test scores were converted to demographically adjusted T-scores ($M = 50, SD = 10$), including adjustments for age, education, gender, and ethnicity as available for each test. In other words, when demographic specific norms were available for a test, T-scores were calculated based on
comparisons to norm groups that shared similar demographic characteristics. Specifically, scores obtained from the Trails B and FAS tests were corrected based on age, education, gender and race/ethnicity (Heaton, Miller, Taylor, & Grant, 2004). Scores obtained from the WCST-64 were adjusted based on age, education, gender and race/ethnicity (Kongs et al., 2000). Scores for the Stroop C test were demographically adjusted for age only (Golden, 1978). The T-scores of tests expected to represent executive functioning were averaged into one score that was meant to reflect the construct or variable, “executive function”. The researcher was granted approval from Pepperdine University’s Graduate and Professional Schools Institutional Review Board (GPS IRB) subsequent to submitting the proposal for consideration and review.

Data Process and Analysis

The Statistical Package for the Social Science (SPSS) version 18.0 was used for all data analyses. For the first research question, a Cronbach’s alpha reliability analysis was conducted to determine whether the four apathy items of the BDI-II would cluster together into a component that could reasonably and meaningfully be viewed as representing apathy. An internal consistency value of 0.7 or higher was expected to indicate that these items adequately cluster together. This cluster of BDI-II items was summed and labeled as “Apathy”. For the second research question, the researchers divided the sample into two groups labeled “Low Apathy” and “High Apathy”. In an effort to maximize apathy differences, the original plan was for the groups to be dichotomized by their Apathy scores as follows: Low Apathy $\leq 33^{rd}$ percentile; High Apathy $\geq 67^{th}$ percentile. Those individuals scoring between the two cut-offs were not to be included in the analysis. This was expected to allow sufficient discrimination to
adequately differentiate between the Low and High Apathy groups. Excluding those individuals scoring between the 33rd and 67th percentile was meant to control for the ambiguity that arises when creating groups based on cut-off scores or median splits. As is described in the Results chapter, the cut-offs had to be adjusted to fit the obtained data.

The executive function variable of interest in the current study consisted of the average of T scores from the four chosen “executive function” measures. A one-way ANOVA was run to determine whether the High Apathy group had significantly lower executive functioning performances than the Low Apathy group. For the final research question, we divided the sample into two groups based on a cluster of total BDI-II items. We labeled these two groups “Low Depression” and “High Depression”. In an effort to maximize depression differences, the original plan was for the groups to be dichotomized by their BDI-II total scores as follows: Low Depression ≤ 33rd percentile; High Depression ≥ 67th percentile. Those individuals scoring between the two cut-offs were not to be included in the analysis. As described in the Results chapter, the cut-off had to be adjusted slightly for the Low Depression group in order to better fit the present data.

A one-way ANOVA was run to determine whether the High Depression group had similar executive function scores compared to the Low Depression group. Finally, correlations were calculated to assess the relationships between executive functioning performance and each of the three components of the BDI-II that were being examined (e.g. Apathy, Non-Apathy, Depression). To determine the correlations between normally distributed continuous variables, Pearson’s r was utilized.
Results

The total sample consisted of 95 individuals. As can be seen in Table 1 and Table 2, on average, the participants who met the inclusion criteria were 55.26 years old ($SD = 5.85$), had a lowest CD4 count of 191.04 ($SD = 198.11$) and had an educational level of 13.67 years ($SD = 2.20$). On the Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001), a reading test that estimates pre-morbid level of intellectual functioning, the participants had a mean standard score of 97.73 ($SD = 17.19$), reflecting an average performance. Table 3 presents the mean values on measures of executive functioning. Consistent with the WTAR finding, participants obtained an overall mean $T$ score of 45.33 ($SD = 9.25$) on the executive functioning measures, indicating that performance fell in the average range.

As indicated in Table 2, the sample was diverse in terms of ethnicity and sexual orientation. The following frequencies were obtained regarding ethnicity: African American ($n = 52$), Caucasian ($n = 30$), Hispanic ($n = 10$), and Biracial ($n = 1$). In regard to sexual orientation, the participants self-identified as follows: heterosexual ($n = 43$), homosexual ($n = 37$) and bisexual ($n = 15$). A majority of the sample had low levels of household income: less than $12,000 ($n = 51$); $12,000 to 49,999 ($n = 35$); $50,000 or more ($n = 7$). A majority of participants were male ($n = 80$) and reported English as their first language ($n = 85$). All participants were proficient in English and were positive for HIV.

The mean Apathy score of the sample was 2.21 ($SD = 2.17$) with Apathy scores ranging from 1 to 8. The mean BDI-II score of the sample was 10.22 ($SD = 8.67$) with scores ranging from 0 to 35. Using the cut-off scores empirically established by Beck
and colleagues (1996), approximately 72% of the sample scored in the range considered as non-depressed (0-13), 11.6% in the range considered mild depression (14-19), 13% in the range considered moderate depression (20-28) and 3.3% in the range labeled as severe depression (29-63).

A Cronbach’s alpha reliability analysis was conducted to determine whether the chosen four apathy items of the BDI-II clustered together into a component that could reasonably viewed as representing apathy. Analysis determined that these items did cluster together with a value greater than 0.7 ($\alpha = 0.748$).

In order to dichotomize the low apathy and high apathy groups, our plan was to use 33$^{rd}$/67$^{th}$ percentile cutoffs to adequately differentiate between the groups. Of the sample, 48.9% ($n = 46$) had an Apathy score of 1 or lower ($M = 0.41$, $SD = 0.5$) and met our revised cut-off criterion for the Low Apathy group while 39.5% ($n = 37$) of the sample had an apathy score of 3 or higher ($M = 4.51$, $SD = 1.5$) and met our revised cut-off criterion for the High Apathy group. The mean apathy score for the Low Apathy group was 0.41 ($SD = .5$) and the mean apathy score for the High Apathy group was 4.5 ($SD = 1.5$). It was examined whether the High Apathy group differed from the Low Apathy group in terms of executive functioning performance. We used an alpha level of 0.05 for all statistical tests. As can be seen in Table 4, a one-way ANOVA, comparing the High Apathy and Low Apathy groups revealed that the High Apathy subjects were no more impaired on the executive functioning measures ($M = 44.87$, $SD = 9.17$), than were Low Apathy subjects ($M = 45.59$, $SD = 10.03$), $t(1,80) = 0.11$, $p = 0.74$. Therefore, the hypothesis that higher levels of apathy would be associated with greater impairment in executive functioning was not supported.
As can be seen in Tables 5 and 6, the Low Apathy and High Apathy groups did not differ significantly in age, lowest T-cell counts or educational level, and gender, income and ethnicity distributions were roughly equivalent. Of note, a difference right at the threshold of statistical significance was found in pre-morbid intelligence as measured by the WTAR with the High Apathy subjects having a lower WTAR standard score ($M = 93.49$, $SD = 18.61$) than the Low Apathy subjects ($M = 101.16$, $SD = 16.08$), $t(1,79) = 3.96$, $p = 0.05$.

A Cronbach’s alpha reliability analysis was conducted to establish the internal consistency of the BDI-II with the present sample. The analysis confirmed a high level of internal consistency reliability ($\alpha = 0.92$), similar to the values reported in the BDI-II manual (Beck et al., 1996). In order to dichotomize the low depression and high depression groups, our plan was to use $33^{rd}/67^{th}$ percentile cutoffs to differentiate the between the groups. Of the sample, $31\%$ ($n = 30$) had a BDI-II score of $4.0$ or lower ($M = 1.90$, $SD = 1.49$) and met our revised cut-off criterion for the Low Depression group, while $33\%$ ($n = 31$) had a BDI-II score of $12$ or higher ($M = 20.39$, $SD = 6.37$), and met our cut-off criterion for the High Depression group. It was examined whether the High Depression group differed from the Low Depression group in terms of executive functioning performance. As can be seen in Table 7, a one-way ANOVA, comparing the High Depression and Low Depression groups, revealed that the High Depression subjects were no more impaired on the executive functioning measures ($M = 45.32$, $SD = 9.49$), than were Low Depression subjects ($M = 44.09$, $SD = 10.95$), $t(1,59) = 0.22$, $p = 0.64$.

To determine whether apathy and depression scores might be differentially associated with executive functioning performance in HIV-infected adults, we calculated
Pearson’s $r$ correlations between three different BDI-II scores (apathy items, total score, and non-apathy related items) and the composite score of executive function. As can be seen in Table 7, and contrary to what the researcher expected, neither apathy nor overall depression scores were significantly correlated with executive functioning performance. Specifically, the correlations between executive functioning and the four-item BDI-II apathy cluster ($r = -0.02$) and between executive functioning and the total BDI-II score ($r = 0.04$) were not significant. Moreover, non-apathy depression items from the BDI-II were also found to be unrelated to the executive function variable ($r = 0.03$).

**Additional Analysis**

The HIV+ individuals ($n = 9$) who were excluded from the present study were analyzed to determine whether those individuals had greater cognitive impairment and/or mood symptoms compared to the individuals who met inclusion criteria. The mean Apathy score of the exclusion group was $2.33$ ($SD = 2.00$) with Apathy scores ranging from 0 to 6. The mean BDI-II score of this group was $12.67$ ($SD = 9.95$) with scores ranging from 0 to 29. On the executive functioning measures, these individuals obtained an overall mean $T$ score of $45.50$ ($SD = 9.48$), reflecting a performance falling in the average range. These data are similar to those of the inclusion group indicating that the HIV+ persons excluded from the sample were no more cognitively impaired or neuropsychologically symptomatic than individuals who met the study’s inclusionary criteria.
Table 1
Demographic Characteristics of Total Sample (N = 95)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>55.26</td>
</tr>
<tr>
<td>Education</td>
<td>13.67</td>
</tr>
<tr>
<td>Lowest CD4 Count</td>
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<tr>
<td>Apathy Score</td>
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<tr>
<td>Depression Score</td>
<td>10.23</td>
</tr>
<tr>
<td>WTAR Standard Score</td>
<td>97.73</td>
</tr>
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</table>

Table 2
Demographic Characteristics of Total Sample (N = 95)

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<th>Ethnicity</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
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<td>1.05</td>
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<td>Asian/Pacific Islander</td>
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<td>1.05</td>
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<tr>
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<td>54.74</td>
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<td>Hispanic</td>
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<td>10.52</td>
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<tr>
<td>White</td>
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<td>Female</td>
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<td>15.79</td>
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<tr>
<td>English as First Language</td>
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<td>Homosexual</td>
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<td>Bisexual</td>
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<td>15.79</td>
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<tr>
<td>Household Income</td>
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<td>28.42</td>
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<td>8.42</td>
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<td>$50,000 or more</td>
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<td>7.37</td>
</tr>
<tr>
<td>Refused To Answer</td>
<td>1</td>
<td>1.05</td>
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Table 3
Executive Function Test Scores of Total Sample (N = 95)

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<thead>
<tr>
<th>Variable</th>
<th>Total Sample</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
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<tr>
<td>Executive Function Score</td>
<td>45.33</td>
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<tr>
<td>Trails B</td>
<td>45.84</td>
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<tr>
<td>FAS Total</td>
<td>48.54</td>
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<tr>
<td>Stroop Color/Word</td>
<td>44.23</td>
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<tr>
<td>WCST 64 Perseverative Errors</td>
<td>46.13</td>
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</tbody>
</table>

Table 4
Executive Function Score Means for Low Apathy (n = 46) and High Apathy (n = 37) Subjects

<table>
<thead>
<tr>
<th>Apathy</th>
<th>Low</th>
<th>High</th>
<th>F</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Function Score</td>
<td>45.59 (10.03)</td>
<td>44.87 (9.17)</td>
<td>0.11</td>
<td>0.74</td>
</tr>
<tr>
<td>Trails B</td>
<td>47.04 (14.11)</td>
<td>44.56 (12.15)</td>
<td>.70</td>
<td>.40</td>
</tr>
<tr>
<td>FAS Total</td>
<td>49.31 (12.19)</td>
<td>47.61 (9.95)</td>
<td>.46</td>
<td>.50</td>
</tr>
<tr>
<td>Stroop Color/Word</td>
<td>43.30 (7.63)</td>
<td>45.11 (9.71)</td>
<td>.86</td>
<td>.36</td>
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<tr>
<td>WCST 64 Perseverative Errors</td>
<td>46.70 (12.19)</td>
<td>45.92 (8.13)</td>
<td>.11</td>
<td>.74</td>
</tr>
</tbody>
</table>

Standard deviations appear in parentheses below means.

Table 5
Demographic Characteristics of Low Apathy (n = 46) and High Apathy (n = 37) Subjects

<table>
<thead>
<tr>
<th>Apathy</th>
<th>Low</th>
<th>High</th>
<th>F</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.78 (7.27)</td>
<td>54.32 (3.80)</td>
<td>3.46</td>
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<tr>
<td>Education</td>
<td>13.78 (2.32)</td>
<td>13.57 (2.21)</td>
<td>.18</td>
<td>.67</td>
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<td>Lowest CD4</td>
<td>218.86 (220.63)</td>
<td>170.67 (164.21)</td>
<td>1.18</td>
<td>.28</td>
</tr>
<tr>
<td>WTAR Standard Score</td>
<td>101.16 (16.08)</td>
<td>93.49 (18.61)</td>
<td>3.96</td>
<td>0.05</td>
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</table>

Standard deviations appear in parentheses below means.
Table 6
Demographic Characteristics of Low Apathy (n = 46) and High Apathy (n = 37) Subjects

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Low Apathy</th>
<th></th>
<th>High Apathy</th>
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<td>N</td>
<td>%</td>
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<td>%</td>
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<td>American Indian/Alaskan</td>
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<td>Black</td>
<td>26</td>
<td>56.52</td>
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<td>Sex</td>
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<td>21.62</td>
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<td>Sexual Orientation</td>
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<td>43.48</td>
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<td>$6,000 to $11,999</td>
<td>23</td>
<td>50</td>
<td>10</td>
<td>27.78</td>
<td></td>
</tr>
<tr>
<td>$12,000 to $24,999</td>
<td>11</td>
<td>23.91</td>
<td>14</td>
<td>38.89</td>
<td></td>
</tr>
<tr>
<td>$25,000 to $49,999</td>
<td>1</td>
<td>2.17</td>
<td>4</td>
<td>11.11</td>
<td></td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>5</td>
<td>10.87</td>
<td>2</td>
<td>5.56</td>
<td></td>
</tr>
<tr>
<td>Refused To</td>
<td>1</td>
<td>2.17</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Answer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 7
*Executive Function Score Means for Low Depression (n = 30) and High Depression (n = 31) Subjects*

<table>
<thead>
<tr>
<th>Depression</th>
<th>Low</th>
<th>High</th>
<th>F</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Function Score</td>
<td>44.09 (10.94)</td>
<td>45.32 (9.49)</td>
<td>0.22</td>
<td>0.64</td>
</tr>
<tr>
<td>Trails B</td>
<td>44.83 (13.80)</td>
<td>46.47 (10.17)</td>
<td>0.29</td>
<td>0.59</td>
</tr>
<tr>
<td>FAS Total</td>
<td>48.91 (12.40)</td>
<td>47.67 (10.42)</td>
<td>0.19</td>
<td>0.66</td>
</tr>
<tr>
<td>Stroop Color/Word</td>
<td>42.21 (7.57)</td>
<td>44.73 (9.73)</td>
<td>1.33</td>
<td>0.25</td>
</tr>
<tr>
<td>WCST 64 Perseverative Errors</td>
<td>43.85 (10.83)</td>
<td>46.90 (9.03)</td>
<td>1.49</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Standard deviations appear in parentheses below means.

Table 8
*Correlations between the Mean Executive Function Score and the BDI-II Apathy, Non-Apathy-Related Items, and Overall Depression Scores (N = 95)*

<table>
<thead>
<tr>
<th>Executive Function Score</th>
<th>Pearson’s Correlation</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apathy Items</td>
<td>-0.02</td>
<td>.87</td>
</tr>
<tr>
<td>Non-Apathy Items</td>
<td>0.04</td>
<td>0.7</td>
</tr>
<tr>
<td>Overall BDI-II Depression</td>
<td>0.03</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Discussion

Overview

The present study sought to examine the relationship between apathy and executive functioning among HIV-infected adults. Additional but related aims were to examine whether specific items of the BDI-II thought to be reflective of apathy would cluster together, and whether there would exist an association between that cluster score and executive functioning performance in a sample of HIV-infected persons. Although apathy in relation to neurocognitive functioning has been evaluated among HIV populations (Anderson & Bergedalen, 2002; Castellon et al., 1998, 2000, 2006; Cole et al., 2007; Paul et al., 2005a), this appeared to be the first study to focus on an older population and to specifically examine individual items of the BDI-II thought to be related to apathy.

Internal Consistency of BDI-II Apathy Items

We hypothesized that the chosen BDI-II items representing apathy would cluster together, and those endorsing a higher number of these items would have lower executive functioning scores compared to those endorsing a lower number of apathy items. The results supported the hypothesis that the BDI-II apathy items would cluster together with an internal consistency of .70 or higher. While this was an encouraging finding, it must be noted that the entire BDI-II has a high level of internal consistency. In fact, the overall internal consistency of the BDI-II was approximately .92 in the present sample. Therefore, the encouraging level of internal consistency among the four items selected for study could not be viewed as definitive evidence that those four items were in fact measuring the construct of apathy. A limitation of the present study, which is discussed
further later in this chapter, was that there was no independent measure of apathy that could be utilized to confirm the extent to which the four BDI-II items represented an adequate measure of the construct of apathy.

**Relationship of BDI-II Apathy Items to Executive Functioning**

The central hypothesis that persons scoring higher on the apathy items would perform more poorly on executive functioning tasks than persons scoring lower on the apathy items was not supported. Inconsistent with our hypothesis, we found that there was no difference in executive functioning performance between those scoring high on our apathy construct and those scoring low on this construct. Therefore, these results do not support the proposition that there is an aspect of depression, similar to apathy and measured by four items from the BDI-II, which is involved with frontal lobe neurological functioning (as measured by neurocognitive tests of executive functioning). Moreover, correlational analysis likewise revealed there was no significant relationship between our four apathy items and executive functioning in the present sample.

**Relationship of BDI-II to Executive Functioning**

Data analysis revealed that there was no significant relationship between BDI-II total scores and executive functioning performance in the present sample. In other words, we did not find a relationship between depressive symptoms and executive functioning. Overall, the sample demonstrated average intellectual functioning, over 13 years of mean education, and relatively low levels of depressive symptoms as measured by the BDI-II. Overall, the present sample was relatively healthy, apparently high functioning, and generally symptom free, both in regard to cognitive and emotional functioning. Additional analyses showed similar levels of health and well-being among
the nine HIV+ individuals who were excluded from participation in the study. This indicated that the lack of neuropsychological symptomatology in our sample was not a mere consequence of the exclusionary criteria applied in the current study. Moreover, the mean age of the sample was approximately 55 and therefore it may be that many individuals in the present sample were not yet old enough or had not been HIV+ long enough to begin to experience significant sequelae in regard to cognitive or emotional functioning.

Another possibility is that the persons in the present sample were actively pursuing treatment regimens that were in fact yielding health benefits, both cognitively and emotionally. The low prevalence of moderate to severe depression (16.3%) and the average executive functioning performance scores found in our HIV+ sample may reflect the advances of HIV care in the post-HAART era. Moreover, our sample was found to be relatively healthy, with an average CD4 count of 190. The sample showed less immune system compromise than found in previous studies of HIV+ individuals, suggesting that perhaps their disease processes and/or symptoms are being effectively managed. The relatively high level of functioning within our sample could therefore represent evidence of the positive outcomes related to HIV treatment advances. It may also be that in our sample of relatively healthy, middle-aged HIV+ persons, any cognitive deficits that did exist may have been too subtle to detect with the methods used in the current study.

Limitations

Overall, we did not find any significant association between apathy and executive functioning in a sample of HIV+ individuals. This is in contrast to findings by Castellon...
and colleagues (2000; 2006) and other recent research showing a relationship between cognitive impairment and symptoms of apathy in neurologically impaired populations (Andersson & Bergedalen, 2002; McPherson et al., 2002; Zgaljardic et al., 2007). The reason for the absence of any significant association between apathy and executive functioning is unclear, but may be due to the methodology employed in the present study. Castellon and colleagues (2006) were able to break down the BDI to suggest that there is an aspect of depression, similar to apathy, which is more likely to reflect potential neurologic involvement. Their subset of seven BDI items was defined as a Mood-Motivation Disturbance factor and it included several items reflective of apathy, as well as items addressing sad mood and irritability. However, most other studies showing a relationship between apathy and cognitive functioning have used independent, validated measures of apathy, such as the Neuropsychiatric Inventory (NPI; Cummings et al., 1994). Therefore, it is suspected that a limitation of the present study was that our apathy variable lacked construct validity and the four BDI-II items we selected failed to adequately capture the construct of apathy. It may be that the four BDI-II items chosen to represent apathy in the present study accounted for too few of the many characteristics that define true apathy. It is also possible that those items were in fact measuring symptoms of depression rather than apathy. Our study failed to utilize an independent, validated criterion measure of apathy to determine whether the four BDI-II items in fact measured apathy. The results of the present study are therefore somewhat inconclusive.

Of note, there was a slight difference, right at the threshold of statistical significance, in estimated pre-morbid intellectual functioning (i.e., WTAR scores) between the Low Apathy and High Apathy subjects. The High Apathy subjects were
found to have a lower mean WTAR score (93.49) than the Low Apathy group (101.16). This finding suggests that pre-morbid intelligence may be a factor (beyond neurotropic effects of HIV) that is related to psychiatric symptomatology such as apathy or depression. This finding also reflects the limitation of the non-experimental archival nature of the current study in which the researcher could not manipulate variables and explore causal relationships. For example, it is possible that some of the psychiatric symptoms and/or frontal/cognitive deficits were pre-existing risk factors leading to HIV contraction, and therefore predated the HIV infection and associated neuropsychiatric sequelae.

As mentioned, a limitation of the current study was that it only utilized the BDI-II as a measure of depressive and apathy symptoms. The self-reported assessment of symptoms of depression and/or apathy on the BDI-II was not corroborated by any other assessment measures or by diagnostic interviews. In the original study, there was no assessment of apathy or depression based on third-party informants (e.g., romantic partners, family members, etc.). Alas, the participants may not have been fully reliable informants in regard to their mood symptoms. It is possible that some participants may not have been able to accurately perceive or have adequate insight to report on their levels of apathy or depression symptoms. Of note, 72% of the sample fell in the non-depressed range. This finding was surprising and not consistent with the relatively high prevalence of depression found among most HIV+ populations that have been studied to date (e.g., Basu et al., 2005; Bing et al., 2001; Chandra et al., 2005; Treisman et al., 1998). One plausible explanation for the low levels of depressive symptoms identified within our sample was the self-report measure utilized. For example, approximately 33%
of the current sample obtained total scores in the range of 0-4 on the BDI-II, suggesting the possibility that some of the sample may have been denying depression, or failing to put forth optimal effort when completing the measure. These findings therefore raise questions about the adequacy of using only a self-report measure to assess for the presence of symptoms of depression and apathy in a community sample of HIV+ individuals. However, the possibility that the present sample, which was relatively small, consisted of an unusual number of persons who were in fact relatively free of depressive symptoms must also be considered.

Another limitation was the method by which the construct of apathy was determined for the present study. Perhaps in part because there were only four BDI-II items utilized to represent apathy, there was a lack of variance between those groups who scored low and those who scored high on this variable. Specifically, only 39.5% of our sample scored in the “High Apathy” range, while 48.9% of the sample scored in the “Low Apathy” range. Therefore, there may have been insufficient representation of High Apathy subjects compared to Low Apathy subjects in the present sample.

A lack of statistical power may also explain why we were unable to find differences between the Low Apathy and High Apathy groups. Because we decided to exclude participants who recently abused substances, and split groups using approximate 33%/67% cut-offs, this yielded a relatively small sample size ($n = 83$), which may have reduced the level of power for detecting executive function score differences between Low Apathy and High Apathy individuals.

It is worth mentioning that one of the four executive function tests (i.e., Stroop C) included in the composite executive functioning performance score was demographically
adjusted solely based on age (Golden, 1978), due to a lack of demographic specific norms. Therefore, the overall executive functioning score was not fully free from potentially significant comorbid factors, including gender, ethnicity, and years of education. Moreover, in regard to executive function scores, in the current study there was no analysis to control for those individuals who may have substituted speed for accuracy. Therefore, there may have been individuals who were speedy and therefore had higher T scores, despite having made a significant number of errors. Failing to account for such errors in our analysis may have compromised the effectiveness of our composite score to adequately capture true executive functioning abilities.

In addition, there were a number of limitations in regards to generalizability. First, because of the relatively small number of participants in the current study ($N = 95$), the findings may not generalize to the greater population of HIV-infected patients. Second, the data were collected in one geographic area and therefore the results may not be generalizable to older HIV+ persons living in other settings. Third, because the current research study examined a population of HIV+ individuals without neurological comorbidities, the results cannot be generalized to an HIV+ population that is expected to have a significant number of such comorbid conditions. Finally, the majority of the subjects in the original study were men, suggesting that the results may not be fully generalizable to women with HIV.

Conclusions and Recommendations

In summary, this study failed to find an association between a subset of BDI-II items thought to be reflective of apathy and executive functioning in a sample of older HIV+ individuals. However, it will be important to further investigate the relevance of
apathy symptoms in samples of HIV-infected individuals, as well as among individuals from other neurologically compromised populations. Based on the limitations of the current study, it is suggested that researchers utilize validated measures of apathy in any future research attempting to examine the relationship of apathy to cognitive functioning. It may be that a relationship between apathy and executive functioning would be found among older HIV+ persons if a more valid and robust measure of apathy were utilized. For example, adaptations of the apathy subscales of the Neuropsychiatric Inventory (NPI), developed by Cummings and colleagues (1994) and modified for use with HIV-infected subjects (Castellon et al., 1998, 2000), may be among the leading measures to be considered for future studies. Moreover, future research should assess apathy through multiple methods rather than rely solely upon self-report. For example, the inclusion of ratings by clinicians and significant others may result in more comprehensive and accurate assessments of apathy.

More research is needed on whether an apathy subscale can be identified from the BDI-II items. The present study utilized the findings from earlier BDI research and rational analysis to select four items as the leading candidates for an apathy subscale. Future researchers might do well to step back and consider whether a broader or different set of BDI-II items could be selected as more promising and valid indicators of apathy among HIV+ persons. Future research might also benefit from the inclusion of more HIV+ persons who display high levels of depressive symptoms, as well as more persons demonstrating significant cognitive problems. Larger samples that have more variance on these critical dimensions of age and functioning may shed greater light on the relationship, if any, of apathy to executive functioning among HIV+ persons.
Despite the lack of findings in the present study, additional research is recommended to further investigate the relationship between the apathy component of depression and its relationship with neurocognitive performance and neurological functioning in an HIV+ population. Further study is needed to clarify whether psychiatric features such as apathy may be a representative biomarker of HIV neurotropic effects on the CNS. Understanding the connection between mood or motivation disturbance and markers of potential CNS involvement is important as it has potential implications for understanding the neurocognitive basis for neuropsychiatric symptomatology. Ultimately, clarifying the connection between psychiatric symptomatology and neurological deficits may lead to the development of more optimal intervention efforts (e.g., neuro-protective therapies and psychopharmacological treatment options) for HIV+ individuals presenting with neuropsychological sequela.
References


