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The Role of Anxiety in Neuropsychological Dysfunction in Early HIV Disease.

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THE ROLE OF ANXIETY IN NEUROPSYCHOLOGICAL DYSFUNCTION IN EARLY HIV DISEASE

A Dissertation

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

The Department of Psychology

by

Joseph Gerald Prejean, Jr.
A. B., Washington University, 1990
M. A., Louisiana State University, 1993
December 1997

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# Table of Contents

Acknowledgments .......................................................................................................... ii  

List of Tables .............................................................................................................. v  

Abstract ............................................................................................................................ vi  

Introduction .................................................................................................................... 1  
  History of HIV ............................................................................................................. 2  
  Pathophysiology of HIV ........................................................................................... 3  
  Physiological Aspects of HIV Disease ........................................................................ 6  
  Neuropsychological Manifestations of HIV Disease ............................................. 9  
  Neuroanatomical Changes in HIV Disease ........................................................... 11  

Specific Areas of Dysfunction .............................................................................. 15  
  Attention and Concentration .................................................................................. 16  
  Language ................................................................................................................ 16  
  Visuospatial Functioning ....................................................................................... 17  
  Verbal Memory .................................................................................................... 17  
  Visual Memory ....................................................................................................... 17  
  Motor Functioning ................................................................................................ 18  
  Global Cognitive Functioning ................................................................................ 19  
  Psychological Components .................................................................................. 23  

Neuropsychological Consequences of Anxiety ............................................. 23  
  Attentional Bias in Anxious Persons ..................................................................... 27  
  Hypotheses ............................................................................................................. 28  

Method ........................................................................................................................ 30  
  Participants ............................................................................................................ 30  
  Materials ................................................................................................................ 31  
  State-Trait Anxiety Inventory .................................................................................. 32  
  Shipley Institute of Living Scale .............................................................................. 32  
  Rey Auditory-Verbal Learning Test ......................................................................... 33  
  Trail Making Test, Parts A and B ............................................................................ 34  
  Block Design ........................................................................................................ 34  
  Grooved Pegboard Test .......................................................................................... 35  
  Digit Span Forward ............................................................................................... 35  
  Controlled Oral Word Association Test .............................................................. 36  
  Paced Auditory Serial Addition Test ....................................................................... 37  

Procedure ................................................................................................................... 37  

Results ......................................................................................................................... 40
List of Tables

1. 1993 Revised Classification System for HIV Infection and Expanded AIDS Surveillance Case Definition for Adolescents and Adults. ................................. 9

2. Demographic Information for the Entire Sample and for Each of the HIV Serostatus Subgroups .................................................................................. 41

3. X² Values Comparing HIV Seropositive and HIV Seronegative Participants at High and Low Anxiety Levels as Determined Using a Tertile Split of Anxiety Scores. .......................................................................................... 42

4. Mean Test Scores (and Standard Deviations) for each Group (as Created Using a Tertile Split of STAI-S Scores and HIV Serostatus) on Dependent Measures. ................................................................. 44

5. X² Values Comparing HIV Seropositive and HIV Seronegative Participants at High and Low Anxiety Levels as Determined Using a Median Split of Anxiety Scores. ............................................................... 45

6. Mean Test Scores (and Standard Deviations) for each Group (as Created Using a Median Split of STAI-S Scores and HIV Serostatus) on Dependent Measures. ................................................................. 46

7. Mean Test Score (and Standard Deviations) by HIV Serostatus Group on Dependent Measures, Controlling for Anxiety Level. ................................. 47

8. Mean appraisals scores per group (as Created Using a Tertile Split of Anxiety Score and HIV Serostatus). .................................................. 48

9. Mean appraisals scores per group (as Created Using a Median Split of Anxiety Score and HIV Serostatus). .................................................. 48

10. Mean Scores (and Standard Deviations) for Each Dependent Variable for Medicated Versus Nonmedicated HIV Seropositive Participants. .... 49

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Abstract

The literature on neuropsychological functioning in patients with asymptomatic HIV disease is widely discrepant with prominent researchers on either side of the debate about whether or not early HIV infection is associated with neuropsychological deficits. Many theories have been put forth to account for these varied results, including inadequate study design, lack of measures sensitive enough to detect differences, and pooling of test scores across individuals that do have deficits, but not necessarily in the same areas.

The present investigation was designed to examine the role of anxiety as a possible confounding variable that could account for differences across HIV serostatus groups. It also investigated the hypothesis that HIV seropositive and HIV seronegative patients differ in terms of their appraisals of their performance and that higher levels of anxiety are related to lowered estimation of performance.

The HIV seropositive and HIV seronegative groups in this investigation did not differ in terms of their neurocognitive functioning. When the groups were further divided in terms of their anxiety level, again there were no differences in their neurocognitive functioning. The investigation therefore failed to identify anxiety as a contributor to neuropsychological dysfunction in HIV seropositive subjects, however, given the lack of HIV group differences in neurocognitive functioning, it did not rule out a potential role for anxiety either.
Further, there was no difference between the groups divided based on HIV serostatus and anxiety level in terms of their ability to accurately appraise their performance. All participants were able to estimate their performances very accurately.

Finally, medication effects were investigated. There were no differences in performance on neuropsychological tests found between the HIV seropositive subjects who followed a medication regimen and those who did not.
Introduction

The latest statistics released by the Centers for Disease Control and Prevention (1996) show that through December 31, 1996, 581,429 people in the United States had been diagnosed with AIDS. Many more persons are living with HIV, but estimates of the number are conservatively skewed because many states do not require health department notification of positive tests for HIV, and many people with HIV have not yet been tested. The largest percentage of AIDS patients remained men who have sex with other men (homosexuals and bisexuals) at 50%, although this percentage has declined since monitoring of the disease began. These numbers demonstrate that although the first cases of HIV transmission were reported in homosexual men, the trend in cases of newly reported HIV infections is away from the homosexual population, and toward IV drug users and their partners. In fact, among women, heterosexual contact and intravenous drug use accounted for 40 and 34 percent, respectively. Of all AIDS cases, 573,800 were adults and adolescents, and 7,629 fell into the category of pediatric AIDS (under 13 years of age). Caucasians accounted for 46.2% of all AIDS cases, 34.9% were African-American, 19.0% were Hispanic, 0.8% were Asians or Pacific Islanders, and 0.3% were American Indians or Native Alaskans. Heyward and Curran (1989) note that the disproportionately large number of cases in African- and Hispanic-Americans can be attributed to intravenous (IV) drug use and sexual relations with partners who are IV drug users, and the percentage of African- and Hispanic-Americans among AIDS cases continues to climb at a faster rate than among any other group.
Through mid-1995 AIDS was listed as the cause of death for 357,598 people in the United States and many more people worldwide, but research continues into ways to halt the spread of the disease, and according to the CDC the death rate from AIDS in 1996 was down 19% from the previous year, probably due to advances in medical care of HIV-seropositive patients ("AIDS Deaths are Down," 1997). The causative agent of AIDS has been established as the Human Immunodeficiency Virus, or HIV, and the means of infection by the virus have been well delineated. The virus is passed from one host to another in the bodily fluids - through shared blood, sexual intercourse, and from mother to child, in utero or through breast feeding (Gallo & Montagnier, 1989). According to Gallo and Montagnier (1989), until a cure can be found, the greatest chance of curbing the epidemic is through knowledge about HIV and its modes of transmission with the expectation that this knowledge will lead to behavioral changes away from risky behavior. A look back at the discovery of HIV is appropriate at this point in order to chart the progress that has been made in the study of this disease.

**History of HIV**

According to all published reports, the first cases of AIDS in the United States were in young homosexual men, and it soon became apparent from their symptoms that they had suffered a loss of T-cells (immune system cells). As in the diseases caused by Human T-cell Lymphotropic Viruses - I and - II, two retroviruses, the immune system was compromised, and like these two viruses, the AIDS pathogen had been shown to be transmitted through blood and sexual intercourse. Because of these commonalities, Gallo and his colleagues (1984) proposed that the agent responsible for AIDS was a
retrovirus related to HTLV-I and -II (Gallo & Montagnier, 1989). Retroviruses differ from other viruses in that their genetic material is RNA rather than DNA. Whereas in all other cells, the flow of genetic information is from DNA to RNA to proteins, the flow is reversed in retroviruses. Information coded in viral RNA is converted into DNA which is then incorporated into the host cell DNA where it is transcribed to messenger RNA, and its proteins are constructed. The retroviruses are able to accomplish this reverse transcription with the help of the enzyme reverse transcriptase.

Early in the history of the study of HIV, several teams of researchers claimed its discovery, variously labeling it, HTLV-III, LAV (Lymphadenopathy-associated virus), and ARV (AIDS associated retrovirus) (Knapp & VandeCreek, 1990). With the development of more sophisticated techniques for investigation, it was determined that all three were the same virus and the name was changed to HIV. HIV is now often referred to as HIV-1 to distinguish it from a structural variant HIV-2 which produces similar clinical symptoms but is primarily seen in Africa (Knapp & VandeCreek, 1990). Because the virus variant most commonly seen within this country is HIV-1, HIV in this paper will refer to HIV-1.

Once HIV was isolated, the next step in the process involved determining its life cycle and the means by which it causes AIDS.

**Pathophysiology of HIV**

HIV is a retrovirus, and as most viruses, it cannot replicate on its own. It therefore needs the DNA of a host cell to carry out its replication in order to produce more viruses. Unlike most viruses, however, because HIV is a retrovirus, it's genetic
material is a single strand of RNA rather than DNA. Therefore, in order to insert its own genetic material into the host cell's DNA an intermediate step must take place, for this conversion of viral RNA to DNA, the virus uses reverse transcriptase.

HIV primarily attacks and destroys T4 immune cells (helper T-lymphocytes) which are at the front lines of the immune system attack on foreign invaders. T4-cells are also often referred to as CD4 cells because of the CD4 receptor on the cell's surface. According to McDougal, Mawle, and Nicholson (1989), it is most helpful to view the infection with HIV in three stages; infection, replication, and consequences for the infected cell. The infection phase begins with binding of the virus to the host cell. The CD4 receptor has an affinity for a protein on the coat of the virus, gp120, and binds tightly to it. Next, the virus merges with the T-cell and uses reverse transcriptase, to transcribe the HIV's RNA into DNA. The DNA is then incorporated into the host cell's genetic structure and there it directs the production of new viral RNA and proteins. The proteins then combine to form new virus particles (replication phase) (Redfield & Burke, 1989). The new viruses then bud from the T-cell membrane and infect other cells. The death of the cell is the ultimate consequence of the infection, but the virus may, for a time, simply impair the functioning of the cell, or the two could live symbiotically until the virus finally kills the cell (McDougal, Mawle, & Nicholson, 1989).

Originally, it was discovered that HIV could kill the helper T-cells by multiplying to great numbers inside them and in that way kill them. This finding led many early researchers to propose that viral replication alone was responsible for the
cell death associated with infection. Since that time, it has been shown that only a small fraction of T-cells display the viral replication necessary for the virus to destroy the host cells, and this number is not sufficient to account for the extreme immunosuppression in AIDS patients. The only way for later researchers to account for the large number of cells killed was to postulate other methods of cell destruction. Several mechanisms have been proposed and demonstrated in vitro, however it is not yet known if these mechanisms actually occur in the body (Redfield & Burke, 1989).

Sodroski, et al. (1986) and Redfield and Burke (1989) have described the formation of syncytia as a possible means to explain the mass destruction of T-cells. In this formulation, the infected T-cells fuse with uninfected T-cells and form massive multinucleated cells that can no longer function properly, and as a result die. Redfield and Burke (1989) also propose that the infected T-cells that are not producing new viral particles may be sought out and killed by the body's natural immune activity. Similarly, they describe a way that even uninfected T-cells might be destroyed by the patient's own body. In a process that is unique to HIV the gp120 proteins that are normally part of the virus can break off and circulate freely in the body. Because the T-cell receptor has such a strong affinity for this protein, it attaches to the free floating gp120. When the immune system recognizes the gp120 as a foreign agent, it destroys the protein and the cell to which it is attached. In this way, healthy T-cells can be destroyed by the immune system of which they are a part.

Additionally, the CD4 receptor is not limited to the T-cells. It is also found on various other cells in the immune system. Hence, the virus can bind to and replicate in
monocytes, macrophages, and similar cells called tissue-dendritic cells found in the skin, mucous membranes, lymph nodes, liver, spleen, and brain (Redfield & Burke, 1989). Apparently these cells are not destroyed by the HIV, but their functioning is disturbed leading to further systemic immunosuppression.

Further complicating this scenario is the fact that it was discovered that the rate of cell death differs between non-activated T-cells and T-cells that have been mobilized to fight infection (Fouchard, Desportes, Reveal, Leonard, Gallo & Zagury, 1986; McDougal, et al., 1985; Redfield & Burke, 1989, Zagury, et al., 1986). Therefore not only are patients more susceptible to infectious agents, but when T-cells are activated to combat these infections, the activation leads to increased replication of the virus and death of the T-cells. Further, when the T-cells are activated to combat the newly invading HIV, this stimulates replication of the virus in the same way that another infection would, leading to the paradox that the body's very means of fighting the disease aids in its proliferation. Regardless of the mechanism of cell death it remains a fact that the T-cell count of the HIV infected patient declines throughout his/her life and eventually the immune system is so thoroughly compromised that it can no longer function.

**Physiological Aspects of HIV Disease**

According to Rogers and Masur (1989), seroconversion to HIV positive status usually occurs between 8 and 12 weeks after the presumed exposure. Upon seroconversion, some patients experience a mononucleosis-like syndrome (Cooper, et al., 1985; Redfield & Burke, 1989). The initial symptoms include fever, fatigue,
swollen glands, sweats, muscle aches, headache, sore throats and often rashes. With treatments, however, these symptoms disappear and the patient returns to a healthy state. Unfortunately the symptoms disappear, but the virus continues to live in the host. The patient can remain in this state for several years, but the next stage of the disease will ensue if the patient does not die of other causes. The patient's lymph nodes also become chronically enlarged (Redfield & Burke, 1989). According to Redfield and Burke (1989) the presence of the overabundance of HIV in the lymph nodes overstimulates B-cells (another type of immune cell) and keeps them in a chronic state of activation, thus causing the lymphadenopathy. Others (Brandon, 1993) have suggested that the virus may be "hiding out" in the lymph nodes and replicating at a high rate, thus accounting for the lymphadenopathy as well as for the latency period after original seroconversion but before symptoms of AIDS appear.

The T-cell count then begins a steady decline and the immune system becomes further compromised. Infectious agents enter the body more easily, and they are harder to fight. At this point with the T-cell count begins dropping rapidly, opportunistic infections, (from normally benign pathogens that may now take advantage of a weakened immune system) begin to appear.

The most recent revision of the CDC classification system for HIV disease (CDC, 1992) greatly increased the number of AIDS cases being reported over previous systems because it takes into account the number of T-cells remaining in a patient that has been diagnosed as HIV positive as well as the number of additional infections that the patient suffers. A discussion of this system is pertinent at this time because it helps
to illuminate the progression of the disease state. The system consists of three categories involving the number of T-lymphocytes the person has, and three clinical categories. The three T cell categories are:

Category 1: > or = 500 cell/microliter of blood
Category 2: 200 - 499 cells/microliter of blood
Category 3: < 200 cell/microliter of blood

The three clinical categories include:

Category A: no condition listed in category B or C and one or more of the conditions listed in Appendix A.

Category B: Symptomatic conditions present that are not included in category C, and the conditions either are attributed to compromised immune functioning, or are of a nature to have a clinical course or require management that is complicated by HIV. Examples of conditions in category B can be but are not limited to those conditions listed in Appendix B.

Category B conditions take precedent over Category A and once a patient has entered Category B, he or she cannot be returned to Category A.

Category C: Includes all clinical conditions listed in the AIDS surveillance case definition (Appendix C). Additionally, Category C conditions take precedence over all others, and once a patient has entered Category C he or she will remain in that category. (See Table 1).
Table 1
1993 Revised Classification System for HIV Infection and Expanded AIDS Surveillance Case Definition for Adolescents and Adults.

<table>
<thead>
<tr>
<th>T cell Categories</th>
<th>A Asymptomatic</th>
<th>B Symptomatic, not A or C conditions</th>
<th>C AIDS-Indicator conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: &gt; or = 500</td>
<td>A1</td>
<td>B1</td>
<td>C1*</td>
</tr>
<tr>
<td>2: 200-499</td>
<td>A2</td>
<td>B2</td>
<td>C2*</td>
</tr>
<tr>
<td>3: &lt; 200 (AIDS-indicator T cell count)</td>
<td>A3*</td>
<td>B3*</td>
<td>C3*</td>
</tr>
</tbody>
</table>

*= Indicates reportable AIDS cases either based on the number of T-cells per microliter of blood, or based on the presence of clinical conditions listed in the AIDS surveillance case definition (Appendix A).

Neuropsychological Manifestations of HIV

Early in the history of AIDS research, several groups had already begun to note neurological deficits that were affecting the long-term survivors of HIV disease (Gopinathan, Laubenstein, Mondale, Krigel, 1983; Herman, 1983; Kermani, Drob, & Alpert, 1984). Initially, it was thought to be the result of a subacute encephalopathy due to cytomegalovirus, but the finding that HIV could enter the brain led to the theory that HIV invades the brain, and disrupts neuropsychological functioning in those who have survived the longest (Navia, 1990). In 1986, Navia and his colleagues (Navia, Jordan, & Price, 1986b) became the first to define what they termed "AIDS Dementia Complex (ADC)." The term AIDS, rather than HIV, was used because at that time, it was not widely known that HIV was the pathogen that caused the immune disorder. The patients that they described were inpatients who demonstrated disturbance of motor
performance, behavior, and global cognitive impairment. Hence the term AIDS Dementia Complex was coined.

According to Perry (1990), the term is a misnomer because patients have been shown to have mental changes without the systemic manifestations of AIDS. Also, these early disturbances may not predominantly involve higher cortical functioning (as in dementia), and the complex of cognitive, motor, and behavioral impairment may not always be present.

In response to criticisms such as Perry's, the American Academy of Neurology AIDS Task Force (1991) has proposed a standard nomenclature for the neurologic manifestations of HIV-1 infection. The task force has separated the complex into two categories. The more severe form, HIV-1-associated dementia complex or HIV-1-associated myelopathy, includes the complex of disturbed motor performance, behavioral changes, and global cognitive impairment sufficient to disrupt social or occupational functioning. A less severe form, HIV-1 associated minor cognitive/motor disorder, describes the situation in which not all of these deficits are present, or in which the disturbance is not great enough to cause impairment in social or occupational functioning. By the current CDC classification system, the manifestations of the severe form are sufficient for a diagnosis of AIDS, while the manifestations of the less severe form are not, although they may be present in persons with AIDS. The task force further states that it is not known at this time if the two forms are the same entity, or even if the minor form will inevitably progress to the severe form. Despite the recommendations of
the task force, however, the term AIDS Dementia Complex has continued to be used in the literature.

Soon after the first reports of ADC, researchers began to elucidate the exact nature of the dysfunction. Investigations were designed to focus on the specifics of the disorder such as timing as well as the exact structures and pathways affected by the pathogen. It has been estimated that neuropathological abnormalities are present in 70% to 90% of the brains of AIDS patients (Ho, Bredesen, Vinters, & Daar, 1989; Vinters, Tomiyasu, & Anders, 1989).

**Neuroanatomical Changes in HIV Disease**

According to Navia (1990), the most frequent structural changes that have been noted on CT and MRI consist of diffuse cerebral atrophy of varying severity, sometimes associated with ventricular dilation. He also noted that these changes have been detected months before the onset of overt dementia. Less frequently, either patchy or diffuse attenuation of the white matter may be observed on CT scans, although MRI is more sensitive in detecting this abnormality. In an earlier paper, he noted that similar changes have also been noted in the basal ganglia and the thalamus (Navia, Cho, Petito, & Price, 1986a). Wesselingh et al. (1993), however, have noted that the structural changes seen are relatively mild, and do not provide a satisfying explanation for the clinical picture.

Characteristic histological changes that have been noted are most often in subcortical structures, primarily in the central white and deep gray matter in the basal ganglia and the thalamus, with relative sparing of the cortical structures (Navia et al.,
1986b). Navia (1990) has reported that positron emission tomography (PET) studies show hypermetabolism of radioactive glucose in subcortical structures early, and both cortical and subcortical structures late. Additional findings have included focal necrosis and vacuolation of the white matter and focal or diffuse demyelination. These changes in brain histology can vary extensively between subjects (Navia, 1990). While HIV likely enters the brain early in the course of the infection (Chiodi et al., 1987), it is unclear when, after the initial insult patients begin to exhibit neurologic impairment. Pathological examination of post mortem patients, however, has shown that the severity of clinical dementia generally correlates with the extent of brain pathology (Navia et al., 1986b). Navia (1990) has also suggested that regional distribution of HIV parallels neuropathy findings, with most infected cells in white and deep gray matter structures, namely the basal ganglia and thalamus.

Along with the CNS changes of the brain, HIV disease also causes structural changes in the spinal cord. As in the brain, the spinal cord suffers similar inflammatory changes, with multinucleated cells and vacuolar myelopathy. These changes have been noted primarily at the thoracic level (Navia, 1990).

It has already been mentioned that HIV is known to enter the CNS early in the course of infection, given that HIV is present in the CSF of individuals in the early stages of HIV disease (McArthur et al., 1989; Sonnerborg et al., 1988). It is not known if the virus enters by itself, or is transported by infected macrophages, as most data suggest that it is the macrophage that is primarily infected (Navia, 1990). There is substantial evidence that HIV-1 has a direct causal role in the pathogenesis of ADC and
ADC is not related to secondary opportunistic infection (Ho et al., 1985; Sidtis et al., 1993).

Productive infection in the brain and spinal cord occurs in the blood-derived macrophages, resident microglia, and multinucleated giant cells (Epstein & Gendelman, 1993), and Geleziunas et al. (1992) have noted that the ability of HIV-1 to localize in the CNS is probably the consequence of macrophage tropism, rather than an affinity for neural tissue. These findings have raised an interesting dilemma in the scientific community, and pose a difficult question that many researchers have attempted to answer. HIV infects relatively few cells in the CNS, yet dysfunction to be accounted for is quite extensive. What is the exact mechanism of tissue destruction that causes the neurologic deficits in HIV disease?

Koyanogi et al. (1987) has suggested that neurotropic variants of HIV may be partly responsible for the clinical and pathological heterogeneity of ADC. Guilian, Vaca, and Noonan (1990) and Lipton (1992) have gone further in suggesting that factors other than direct infection may play a role in the development of neural cell dysfunction, and others have agreed.

It is generally held that productive HIV infection is restricted to the macrophage, and cell loss is relatively absent. Because the degree of neurologic impairment is out of proportion to the neuropathy, many researchers today feel that brain injury could be due to secondary metabolic processes that result from the HIV infection (Hall et al., 1991; McArthur, 1994; Navia, 1990).
Prevailing theories have included destruction of HIV infected neural tissue, and other variations of the theory of immune modulated cell destruction. Navia (1990) has suggested that neuronal dysfunction could be the result of macrophage destruction of latently infected neural cells, or the release of substances that are toxic to surrounding tissues. The majority of researchers have followed the latter course in their investigations. Immune system markers such as β2 microglobin (Elovaara et al., 1989), quinolinic acid (Heyes et al., 1991), tumor necrosis factor α, and interleukin-6 (Tyor et al., 1992) have all been implicated. All of these markers of immune functioning have been found in the CSF of HIV seropositive patients. Wiley et al. (1992) have claimed that CSF findings correlate well with one another, but not with the extent of HIV in the brain, but Heyes et al (1991) have reported that when opportunistic infections are controlled for, levels of quinolinic acid (a macrophage product of tryptophan metabolism) parallel neurologic dysfunction. Further, the cytokines IL1, and TNFα have been shown to damage neural cells in in vitro cultures (Guilian & Lachman, 1985; Selmaj & Raines, 1988). Additionally, β2 microglobins and quinolinic acid levels in the CSF fall with Zidovudine (AZT; an antiretroviral medication) therapy (Brew et al., 1989; Heyes et al., 1991). AZT at least temporarily disrupts HIV replication, and given that AZT has been shown to ameliorate ADC (Portegies et al., 1993; Portegies et al., 1989; Schmitt et al., 1988; Sidtis et al., 1993), this is an important finding suggesting that HIV replication in the brain, and therefore production of the immune modulators plays an extensive role in neurological dysfunction.
Another theory of neuronal destruction in HIV disease comes from Epstein and Gendelman (1993). They suggest that HIV-1 infected macrophages can initiate neurotoxicity, which is then amplified through cell to cell interactions with the astrocytes. This theory has not received extensive attention in the literature.

Finally, there is clinical, imaging, and pathologic evidence that dopaminergic neural dysfunction may be involved in the progression of ADC (Kieburtz et al., 1991). First, a hallmark of ADC is motor impairment. Secondly, Kieburtz et al. (1991) found that their patients were responsive to L-Dopa, although dopaminergic side effects developed rapidly suggesting that dopamine receptors were significantly upregulated. Finally, when dopamine blockers were given, ADC patients developed Parkinson-like symptoms.

**Specific Areas of Dysfunction**

While it has been accepted that a majority of AIDS patients will eventually experience the neurological symptoms of HIV, the timing of the dysfunction has been the subject of considerable debate. Several studies have reported that the decline in functioning begins early in the disease, with early loss of cognitive functioning being gradual and often overlooked (Navia, 1990), and greater neuropsychological dysfunction with increasing severity of HIV disease. For example Grant et al. (1987) reported that in their sample, nine percent of seronegative controls, forty-four percent of asymptomatic seropositives, fifty-four percent of patients with AIDS related complex, and eighty seven percent of AIDS patients experienced some form of neuropsychological dysfunction. Others (Janssen et al, 1988; Perry, Belsky-Barr, Barr,
& Jacobsberg, 1989; Wilkie, Eisdorfer, Morgan, Lowenstein, & Szapocznik, 1990) have also argued that asymptomatic HIV positive patients are more likely than seronegative controls to demonstrate deficits in performance.

Attention and Concentration. Although Stern, et al. (1991) have argued that there are no deficits in the areas of attention and concentration, using the Paced Auditory Serial Addition Test, Grant et al. (1987) has shown that there are indeed deficits in divided attention. Further, Navia (1990) has stated that patients who have retained insight into their illness, have complained of concentration problems stating that tasks require much more time, and are laborious. In order to comprehend when reading, patients must reread pages several times, and often lose their trains of thought during conversations. Finally, he reported that patients become bewildered and confused when presented with more than one task simultaneously.

Language. Generally, those researchers that have studied language functioning have concluded that patients retain intact language functioning throughout their illness. Using a confrontational naming task (the Boston Naming Test) and a word generation test (Thurstone Word Fluency), several researchers report that symptomatic HIV positive subjects performed as well as seronegative controls (Claypoole et al., 1990; Goethe et al., 1989; Janssen et al., 1989; Miller et al., 1990; Ollo, Johnson, & Grafman, 1991; Ollo & Pass, 1988; Stern, Sano, Williams, & Gorman, 1989; Tross et al., 1988; van Gorp, Miller, Satz, & Visscher, 1989; Wilkie et al., 1990). Contrary to these reports, however, Perry et al. (1989) and Stern et al. (1991) report deficits in word
generation, and Saykin et al. (1988) have found HIV seropositive patients to have difficulty on the Boston Naming Test.

**Visuospatial Functioning.** As with most domains of functioning, the results are split in the area of visuospatial functioning. On the Block Design subtest, Tross et al. (1988) and van Gorp et al. (1989) have found differences between their HIV seropositive subjects and controls. Using the Rey-Osterrieth Complex Figure Test, however, Poutiainen, Iivanainen, Elovaara, Valle, and Lindevirta (1988) and van Gorp et al. (1989) were unable to corroborate these results.

**Verbal Memory.** In the area of verbal memory functioning, Jansenn et al. (1989) and others (Saykin et al., 1988; Wilkie et al., 1992) noted differences between HIV seropositive and HIV seronegative subjects on the prose section of the Wechsler Memory Scale. Likewise, several investigators have reported deficits in their HIV seropositive subjects on the Buschke Selective Reminding Test (BSRT; Stern et al., 1989; Stern et al., 1991; Wilkie et al., 1990). Unfortunately as in other domains of functioning, in the area of verbal memory, a number of studies contradict the findings of the previous researchers. Using the Rey Auditory Verbal Learning Test and the California Verbal Learning Test, Ollo and Pass (1988) and van Gorp et al. (1989) did not find differences between HIV seropositive and HIV seronegative subjects. Likewise, with the BSRT, Claypoole et al. (1990) and Goethe et al. (1989) failed to note any differences.

**Visual Memory.** Similarly, results of testing are mixed in the area of visual memory, with several researchers reporting deficits on the Visual Reproduction section
of the Wechsler Memory Scale (WMS; Olio & Pass, 1988; van Gorp et al., 1989), the Rey-Osterrieth Complex Figure Test (van Gorp et al., 1989), and the Digit Symbol subtest of the Wechsler Adult Intelligence Scale - Revised (Janssen et al., 1989). For every study that reports a difference in performance between HIV seropositive and HIV seronegative subjects, it seems that another reports the opposite. For example, using the WMS, Grant et al. (1987), Poutiainen et al. (1988), Saykin et al. (1988), and Tross et al. (1988) did not find the differences reported by other researchers. Additionally, using the Benton Visual Retention Test and the Tactual Performance Test, Saykin et al. (1988) failed to find deficits among their HIV seropositive subjects.

Motor Functioning. Using tests of simple psychomotor functioning, several researchers (Claypoole et al., 1990; Franzblau et al., 1991; Goethe et al., 1989; Olio et al., 1991, Stern et al., 1991) were unable to find the motor deficits that are seen as a hallmark of neuropsychological dysfunction in people with HIV associated dementia. Others, however, reported differences between HIV seropositive and HIV seronegative subjects (Miller et al., 1990; Saykin et al. 1988; Tross et al., 1988). On tests of motor speed, and information processing, results were equally divergent. According to van Gorp et al. (1993), the majority of studies using the Trail Making Test part A failed to report any deficits in functioning. By contrast, about half of the studies using Trails B have found differences between their HIV seropositive and HIV seronegative subjects. Other researchers reported differences in choice reaction time, although not in simple reaction time (Perdices & Cooper, 1989; Wilkie et al. 1990; Wilkie et al., 1992). Van Gorp et al. (1993) attributed these deficits to cognitive slowing rather than simply to
motoric factors. They claimed that the "slowing of psychomotor functions where thought is wedded to action may be the cardinal feature of HIV encephalopathy" (p. 171).

Global Cognitive Functioning. In the area of higher cortical functioning, Claypoole et al. (1990), Grant et al. (1987), and Stern et al. (1991) all noted deficits on tasks of abstract reasoning, whereas the findings of Rubinow, Berettini, Brouwers, and Lane (1988) and Saykin et al. (1988) contradicted these results. Poutiainen et al. (1988), Rubinow et al. (1988), and van Gorp et al. (1989) reported that intellectual functioning was disturbed, and Stern et al. (1989), Stern et al. (1991) and van Gorp et al (1989) all reported low scores on the Mini Mental State Exam.

While it is generally accepted in the scientific community that people in the late stages of HIV disease are susceptible to neurologic complications, not all researchers agree that deficits are manifested early in the disease process. For example, several researchers (Goethe et al., 1989; McArthur et al., 1989; Miller et al., 1990; Tross et al., 1988) reported that their investigations revealed no differences between their asymptomatic HIV seropositive patients and HIV seronegative controls. In 1988, the World Health Organization (cited in van Gorp et al., 1993) stated that there is "no evidence that otherwise healthy [HIV seropositive] individuals are more likely to be functionally impaired than persons not infected with HIV." Selnes et al. (1990) even stated that after a follow up of one and one half years there were still no differences between HIV seropositive and HIV seronegative subjects. However, in a recent review of the literature, White, Heaton, Monsch, and the HIV Neurobehavioral Research
Center Group (1995) compared the 57 studies of HIV and neuropsychological impairment performed to the time of their review and found that according to these investigations 35% of HIV seropositive participants evidenced some form of neuropsychological deficit as compared to only 12% of HIV seronegative controls in these studies.

According to van Gorp, and colleagues (1993), the general consensus among HIV researchers is that HIV penetrates the blood-brain barrier shortly after infection, and that some individuals will then evidence acute encephalopathic or meningitis-like symptoms. Most people, however, show no dysfunction immediately. Although a subsample of individuals will later develop ADC, it is not known what determines the progression of the dysfunction. Some factors that have been suggested are (1) genetic susceptibility of the host, (2) degree of immunosuppression, and (3) whether the variant of HIV is neurotropic (Navia, 1990). Satz (cited in van Gorp et al., 1993) also suggested that a determining factor of whether deficits will be found is education level. They concluded that those studies which found no differences in cognitive functioning used subjects with a high level of education and that the differences between asymptomatic HIV seropositive patients and seronegative patients were greater among the less educated. This contention was supported by investigations of the cognitive reserve hypothesis (van Gorp et al 1994; Picano & Klusman, 1993; Salmon, 1994; Stern, 1994). The work on cognitive reserve suggests that higher education levels provide a buffer to loss of functioning, implying that those patients with higher educational levels can lose more of their cognitive capacity before showing deficits (Picano & Klusman, 1993),
although this may be accounted for by the low test ceilings on many neuropsychological measures. Van Gorp et al. (1993) have concluded that although some studies have shown impairment it is usually not enough to affect daily functioning, but that infected people with less education are at greater risk for such a loss.

It is not disputed that in late stages of HIV disease individuals encounter a decline in functioning. The amount of decline is much less clear in the early stages. Previously cited studies were primarily of subjects in the end stages. With regard to studies involving subjects in the early, asymptomatic phase of their illness, for every investigation which finds deficits early on, there is generally another to dispute it. Seines et al (1990) offered several possible explanations for these discrepant findings. First, they noted that in most early studies which reported differences between asymptomatic HIV seropositive subjects and HIV seronegative subjects, the samples were very small and differences could have been due to chance. In larger studies (Goethe et al., 1989; Mauri, Sinforniani, Muratori, Zerboni, & Bono, 1993; McArthur et al., 1989; Tross et al., 1988), asymptomatic HIV seropositive subjects did not differ significantly from HIV seronegative controls.

Also, in the early studies, education level was poorly controlled (Selnes et al., 1990). In those studies, the HIV seropositive sample tended to be much less educated than controls. Heaton, Grant, and Matthews (1986) and Selnes et al. (1990) indicated that educational levels accounted for significant variance in neuropsychological functioning. Picano and Klusman (1993) asserted that brain reserve capacity (BRC) may moderate neuropsychological abnormality as HIV disease progresses and may
partially account for the variability in neuropsychological impairment observed in early stages of HIV infection. To get an accurate picture of neuropsychological changes throughout the course of HIV disease one must ensure that the sample size is adequate and the control group is fairly equally matched to the sample. Finally, it is important to use tests that have been shown to be sensitive to the deficits that are typical of HIV seropositive subjects (Newer, Miller, Visscher, & Satz, 1991).

White and her colleagues also outlined other possible explanations for the discrepant results including differences in mode of infection of participants and length of battery of tests. Studies of intravenous drug users tend to find loss of functions more often than investigations which look at only gay men. Battery length, they argued, affects results because brain areas affected by the virus vary between individuals, as do the difficulties that result. Therefore investigations that compare subjects on only a few tests will be less likely to find positive results when trying to uncover deficits because many of the subjects are likely to be impaired in one or more areas that may not be tested.

Consistent with the report of White and her colleagues (1995), Heaton et al. (1995), using an 8-hour test battery, compared subjects on the presence or absence of impairment (defined as below average functioning in 2 or more domains) rather than comparing subjects in specific areas of functioning. Using this more global definition of impairment they reported increased rates of impairment at each successive stage of HIV infection in their sample of 500 men. They carefully point out, however, that although
30.5% of their subjects evidenced some form of neuropsychological impairment, almost 70% of subjects did not.

Although the exact timing of deficits has been disputed, it is not questioned that HIV patients will frequently demonstrate neuropsychological decline as their illness progresses. Deficits have been mainly characterized as subcortical in nature with dysfunction in the areas of psychomotor functioning, behavior, memory, and cognitive performance (Navia et al., 1986b; Price et al., 1988). However, several other areas that have been investigated have revealed deficits.

**Psychological Components.** Relatively few studies in the literature have reported changes in psychological status. Increased depression in HIV seropositive subjects has been infrequently mentioned (Miller et al., 1990; Poutiainen et al., 1988), and the majority of studies reported no differences in mood between HIV seropositive and HIV seronegative subjects (Ollo & Pass, 1988; Perdices & Cooper, 1989; van Gorp et al., 1989). Noting that a typical complaint of HIV seropositive subjects is dysphoria, van Gorp suggested that negative findings regarding mood may be due to selection bias in many studies. Perhaps people who were depressed did not volunteer to participate. Neuropsychological deficits in HIV seropositive subjects, however, cannot be accounted for by depressed mood (Grant et al., 1993). Likewise, in the area of anxiety, reports have been sparse.

**Neuropsychological Consequences of Anxiety**

The topic of the effect of emotional state on test performance has been a subject of considerable investigation. In particular, depression is frequently considered to have
an impact on performance on neuropsychological tests (Gass & Russell, 1986; Heaton & Crowley, 1981; Hinkin, et al., 1992; Sackheim, et al., 1992). However, while depression has been studied for its potential effects, the literature has largely ignored the investigation of anxiety as an impediment to test performance.

Even undergraduate psychology majors are familiar with the inverted "U" of Yerkes and Dodson (1908) in which a graph of test performance follows an inverted "U" shape when performance is plotted on the y-axis, and anxiety is plotted on the x-axis. At very low levels of anxiety, performance is poor due to lack of arousal or motivation. As anxiety increases, arousal increases, and test performance rises proportionately, but past a certain point the anxiety begins to interfere with performance by narrowing the focus of attention so that the individual becomes fixated on certain stimuli while relatively ignoring the rest. Performance then begins to decline with increasing anxiety.

While the Yerkes-Dodson Law has been demonstrated in the laboratory, and most people can probably think of examples from their own lives, the study of the neuropsychological consequences of anxiety has not progressed far beyond this point. Even in the investigations of anxiety, researchers have typically limited themselves to the investigation of specific anxiety disorders - anxiety as a trait- rather than to state anxiety. Additionally, positive results have typically been reported when using tasks in which the anxious subjects' attention was drawn to stimuli relevant to their particular anxiety situation.
Burgess and colleagues (1981) used a dichotic listening shadowing task to demonstrate that agoraphobic and social phobic subjects detected a greater number of target words (words with phobic relevance) presented to the unattended channel than did controls. Foa and McNally (1986) conducted a similar investigation with obsessive-compulsive patients and achieved corroborating results. These studies provide evidence for an attentional bias in anxiety disorders.

Other researchers have demonstrated that attention can be drawn away from ongoing task demands and toward threat cues in the environment (Matthews & MacLeod, 1986; MacLeod, Matthews, & Tata, 1986). Reaction times to to-be-detected visual probes were longer if the probe coincided with a threat word in a different channel (auditory) (Matthews & MacLeod, 1986). In the second study, shorter reaction times resulted when subjects were required to report the location of a dot on a screen if the dot appeared in the same place where an anxiety related word had been (MacLeod, et al., 1986). These, and other investigators have used a modified Stroop task to show that color naming latency was longer for threat words than for non-threat words (Geller & Shaver, 1976; Matthews & MacLeod, 1985).

However, it seems that while attentional capacity is preferentially drawn to threat words over neutral stimuli, researchers have failed to find a threat bias in recall and recognition trials. In fact, Mogg, Matthews, and Weinman (1987) found that anxious subjects had a higher recognition rate for non-threat words, than for threat words.
While it is not questioned that attention is drawn to anxiety provoking stimuli in subjects with anxiety disorders, on neuropsychological tests measuring constructs other than attention, the anxiety disorders appear to play much less of a role. For example, Zalewski, Thompson, and Gottesman (1994) failed to find differences between the performance of veterans with Post Traumatic Stress Disorder, Generalized Anxiety Disorder, and control veterans on such measures as the Wechsler Adult Intelligence Scale - Revised (WAIS-R; Wechsler, 1981) Block Design subtest, the California Verbal Learning Test, the Rey-Osterrieth Complex Figure Test, and the Paced Auditory Serial Addition Test.

Gass, Ansley, and Boyette (1994), however, suggest that state anxiety, rather than anxiety disorders may be associated with preoccupations, intrusive thoughts, inattention, distractibility, and anxiety over possible failure. They have demonstrated that scores on maze performance and fluency tests (both verbal and non-verbal) are mildly associated with a measure of GAD and strongly related to a Minnesota Multiphasic Personality Inventory - 2 measure of fearfulness. Likewise, Buckelew and Hannay (1986) demonstrated that performance on the Block Design subtest of the WAIS-R (Wechsler, 1981) and word fluency tests were sensitive to state anxiety and Mueller, (1979, cited in Lezak, 1983) and Pyke and Agnew (1963) found decreased abilities on the Digit Span Forward subtest of the WAIS-R in their anxious subjects. King and colleagues have also shown that lower scores on the Finger Tapping Test and higher times to completion on the form board were related to higher trait anxiety (King, Hannay, Masek, & Burns, 1978).
Impairment in cognitive functioning has been a consistent complaint of patients with anxiety disorders, and is even listed as a criterion for the diagnosis of PTSD (American Psychiatric Association (APA), 1994). According to the authors cited above, these complaints may be justified.

**Attentional Bias in Anxious Persons**

The attentional bias produced by anxiety clearly leads to cognitive deficits, but it seems equally likely that global deficits may be produced, or at least exaggerated, by the anxious person due to hypervigilance to any loss. In the medically compromised patient experiencing even slight cognitive decline, anxiety about the losses may lead to a misinterpretation of normal test errors as an indication of decline.

Several investigators have noted the negative impact of mood on appraisal of cognitive performance in HIV seropositive people. In fact, Perry (1990) reported that HIV seropositive people’s metacognitions indicate that they feel that their deficits are worse than they actually are measured to be. And van Gorp et al. (1991) reported that depression is associated with increased cognitive complaints (including forgetting appointments and experiencing the tip of the tongue phenomenon), but the number of complaints is unrelated to actual deficits. Further, Wilkins et al. (1991) reported that although 49% of their subjects reported cognitive complaints, the complaints were associated with psychiatric symptoms (including depression and anxiety), but again, not with cognitive performance. Van Gorp and colleagues (1993) summarized the relation of mood to report of cognitive complaints stating that subjective report of cognitive failures may be more related to an individual’s current affective state rather than to
objective neuropsychological difficulties. However, more recently, Poutiainen and Elovaara (1996) have clarified this relation with regard to stage of HIV infection, stating "in symptomatic infection 'subjective' complaints may reflect 'objective' cognitive deficits, whereas for asymptomatic subjects there may be other reasons for such complaints," (p. 224). These studies indicate that anxiety may impact appraisal of performance in situations where it does not directly influence performance.

Hypotheses

The current study will attempt to further elucidate the role that anxiety plays in the neuropsychological dysfunction in early HIV disease. Given the disparate findings in the research literature on HIV seropositive people in the early stages of disease, it is possible that with tighter control over previously uncontrolled variables, a clearer picture of the neuropsychological sequelae in early HIV disease may emerge; suggesting that one or another of these variables may have impacted and confounded previously reported results. One variable that has not received extensive attention in the HIV literature has been anxiety. Therefore, it is necessary that before the neuropsychological deficits in HIV disease be attributed directly to the effects of HIV, the possibility that anxiety plays a role in neuropsychological dysfunction in early HIV disease must be examined. Hypotheses to be researched in this investigation include: 1) HIV seropositive participants will evidence significantly lower performance scores on neuropsychological measures said to be sensitive to HIV serostatus than their HIV seronegative counterparts, regardless of anxiety level. A main effect is expected for HIV serostatus for those neuropsychological measures previously shown to be disturbed.
in people with HIV. 2) Participants high in anxiety will perform more poorly on those
tests which are sensitive to increased anxiety (a main effect for anxiety level). 3) An
interaction between HIV serostatus and anxiety level is expected for performance
appraisal scores. The participants high in state anxiety will judge their performances on
neuropsychological measures to be lower than their actual scores, and that this
difference will be exaggerated in those individuals with HIV. These findings would
suggest that neuropsychological deficits which are seen early in HIV disease are not due
to anxiety but likely are related to the direct effects of HIV on cognitive functioning,
and that anxious participants would have a tendency to exaggerate their self-report of
the deficits that they do experience.
Method

Participants

This investigation received approval from the Louisiana State University Medical Center Institutional Review Boards and the Louisiana State University Institutional Review Board. Seventy-six participants were recruited from the HIV Outpatient (HOP) Clinic at Medical Center of Louisiana at New Orleans (MCLNO) in New Orleans, Louisiana. Thirty-eight clinic patients composed the experimental group, and the control group was made up of HIV seronegative friends or relatives of HIV seropositive individuals seen at this clinic (N = 11) or elsewhere (N = 27). This control group was chosen in order to maximize the similarities to the experimental group in terms of demographics and anxiety level. No monetary or other compensation was offered to the subjects. Potential risks (no serious risks) and benefits (aid in future treatment of HIV patients) of the study were explained, and participants were instructed that they could request information on the results of the study, and this information would be forwarded to them after completion of the study.

Because this study focused on asymptomatic HIV disease, subjects were excluded if their T-cell count was lower than 200 CD4/mm³ of blood, or if they had begun to show systemic complications of HIV disease (qualifying for a diagnosis of AIDS). All HIV seropositive individuals fell into CDC categories A1, A2, B1, or B2. Potential participants were also excluded if they had abused recreational drugs or alcohol within the preceding six months, as defined by DSM-IV (APA, 1994) criteria, or if they were unable to achieve a sixth grade reading level on the Wide Range...
Achievement Test Revision Three (WRAT-3; Wilkinson, 1993). Attempts were made to equate all groups on the basis of race, age, sex, education level, and intellectual functioning.

Materials

Dependent variables were derived from neuropsychological measures which were selected because they have been shown to be sensitive to performance decrements among subjects with HIV or anxiety. The neurocognitive areas selected for assessment were based on their vulnerability to HIV infection included attention and concentration (Paced Auditory Serial Addition Test), learning and memory (Rey Auditory Verbal Learning Test), psychomotor speed (Grooved Pegboard), verbal fluency (Controlled Oral Word Association Test), and information processing (Trail Making Test Part B). Neuropsychological measures sensitive to anxiety included tests that are very difficult or elicit the greatest amount of state anxiety (Buckelew & Hannay, 1986) (e.g., Block Design and Digit Span Forward from the Wechsler Adult Intelligence Scale - Revised and the Paced Auditory Serial Addition Test). Additionally, a measure of anxiety (State-Trait Anxiety Inventory - State form) was utilized to determine group placement, and an estimate of intellectual functioning (Shipley Institute of Living Scale) was employed as a control variable.

A final dependent variable was the accuracy of the participants appraisal of his or her neuropsychological functioning. After administration of each of the neuropsychological measures, subjects were asked to estimate their performance on that test on a scale of below average, average, or above average. For each measure, a
score of -2, -1, 0, 1, or 2 was assigned based on the comparison of the participant's appraisal to his or her actual performance level. A score of -2 indicated an appraisal of below average for an actual above average performance (the subject appraised his or her performance to be 2 steps below his or her actual performance). Subjects who appraised their performance one step below their actual performance were given a score of -1. Correct appraisals obtained a score of 0, while overestimates of actual ability received scores of 1 or 2 depending on the extent of their overestimates. Negative appraisal scores were summed and the absolute value of this sum constituted a dependent variable defined as the extent of the underestimation of his or her performance (NEGAPP). Likewise, positive appraisal scores were also be summed to yield a dependent variable for the level of overestimation of performance (POSAPP).

The following measures were used in this investigation.

State-Trait Anxiety Inventory. (STAI; Spielberger, 1983). The STAI assesses both level of anxiety symptoms at the time of administration (the state portion, STAI-S), as well as the examinee's general level of anxiety (the trait portion, STAI-T). Only the STAI-S will be used for this study. The STAI-S has been shown to be internally consistent (median alpha coefficient of .92) and concurrently valid (correlation of .77 to .84 with other anxiety measures). However, test-retest reliability is low (.16 to .62) which reflects fluctuation in anxiety states over time (Spielberger, 1983).

Shipley Institute of Living Scale. (SILS; Shipley, 1946). The SILS is a paper and pencil test consisting of two parts. The first, the verbal section, is a multiple-choice test that involves picking from four choices the best synonym for each of the test words.
The second part is a free response test of abstract reasoning in which the subject must complete several incomplete series (for example, the subject may be given the series 1,2,3,4, and will be asked to fill in the blank). The Shipley total score (Verbal and Abstract quotients) provides estimated WAIS (Wechsler, 1955) and WAIS-R (Wechsler, 1981) IQ scores and was used as an estimate of intellectual functioning in this investigation. Reliability estimates for the Shipley total score range from .78 for test-retest reliability to .92 for split-half reliability. Although heavily verbally weighted, the Shipley total score has shown a median correlation of .79 with the WAIS (range of .73-.90 across 11 studies) and correlations of .74 and .85 with the WAIS-R (Zachary, 1986).

Rey Auditory-Verbal Learning Test. (RAVLT; Rey, 1964; Lezak, 1983). The RAVLT involves verbal presentation of a list of fifteen nouns (list A) to the examinee who is then asked to repeat the list back to the examiner in no particular order (free recall portion). After five presentations of the list, a second list of fifteen nouns (list B) is presented as an interference trial, followed by a free recall test of this list. Immediately following recall of list B, the original list is requested again to assess interference. After twenty minutes, free recall of list A is again tested (delayed recall). The RAVLT is well normed for ages thirteen through above seventy and demonstrates a test-retest reliability of .55 at one year intervals (Snow, Tierney, Zorzitto, Fisher, & Reed, 1988). Alternate forms of the RAVLT correlate in the range of .60 to .77, and in factor analytic studies, the RAVLT learning measures correlate .50 to .65 with other learning measures (Lezak, 1995). The RAVLT is generally regarded as a measure of

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episodic verbal memory, and is well-normed nationally as well as regionally using subjects from Louisiana (Savage & Gouvier, 1992). For the purposes of this study, the total recall for trials 1-5 (RAVLTTOT), and the recall on the delay measure (RAVLTDLAY) were used as dependent variables.

**Trail Making Test, Parts A and B.** (TMT; Army Individual Test Battery, 1944). The TMT assesses visuospatial search skills, psychomotor speed, and the examinee's ability to alternate between cognitive sets within a task (divided attention). The test involves connecting a series of circles in numeric order (Part A) and alternating alphanumeric order (Part B). In part A the circles are labeled with numbers and must be connected in order from lowest to highest number. Part B employs both numbers and letters, and the circles are connected in ascending order, alternating between numbers and letters. Reliability coefficients for the TMT have ranged from .46 to .98 for part A and .44 to .92 for part B (Spreen & Strauss, 1991). Lower reliabilities were from studies assessing test-retest reliability in which scores would be expected to improve and reliabilities would therefore be lower. Higher reliability ratings were from alternate forms. These findings would seem to indicate strong practice effects. The TMT has been found to be highly sensitive in detecting brain damage (Dodrill, 1978; O'Donnell, 1983). The test yielded 2 dependent variables, TMTA, which was the time to completion for Part A of the TMT, and TMTB, the time to completion for Part B of the TMT.

**Block Design.** (BD; Wechsler, 1981). This test involves the use of cubes that are red on two sides, white on two sides, and half red and half white on two sides. The
participant is first given four cubes to replicate specific designs. As the test progresses in difficulty, the participant is given nine blocks to construct more complex designs. Split-half reliability ranges from .83 for 55-64 year old participants to .89 for participants aged 25-44. The BD test has also been shown to be sensitive to high levels of anxiety (Buckelew & Hannay, 1986). The participant is given 2 chances to correctly replicate each of the first 2 designs, and is given 2 points for a correct response on the first attempt, and 1 point for a correct response on the second attempt. The participant receives at least 4 points for each design correctly replicated after the initial 2 designs. Partial credit is not given, however, bonus points are added for speed of performance. The dependent variable (BLOCKS) obtained from this measure represented the participant’s total score on the measure.

**Grooved Pegboard Test.** (GPT; Kløve, 1963; Matthews & Kløve, 1964). This test requires fitting ridged pegs into a board containing a five by five grid of slotted holes rotated at various angles. Normally the time to completion for each hand is scored. The GPT assesses motor slowing or clumsiness and provides measurements for both the dominant and non-dominant hands (Miller et al., 1990). Kelland and colleagues (1992) found substantial test-retest reliability ($r=.82$) with this measure. This test also yielded two dependent variables, GPTD, the time required to complete the test using the participant’s dominant hand, and GPTN, the time to completion using the non-dominant hand.

**Digit Span Forward.** (DSF; Wechsler, 1981). On this test that is generally regarded as a measure sensitive to attention and concentration, the examiner reads
aloud a series of digits at a rate of one per second. After the last digit in the series has been read, the participant must repeat the digits to the examiner in the exact order in which they were presented. The number of digits presented increases as the test progresses. The participant is given 2 chances to correctly repeat a sequence at each of the specified string lengths. For each string that is correctly repeated, the participant is awarded 1 point. The second attempt at each string is administered and scored regardless of the participant’s success or failure on the first attempt. The test ends when the participant fails to correctly repeat both strings at a given length. Split-half reliability coefficients range from .70 for 16-17 year olds to .89 for 25-34 year olds. Performance on the DSF has been shown to be sensitive to anxiety (Mueller, 1979 cited in Lezak, 1995; Pyke & Agnew, 1963), and is generally not affected in persons with HIV disease (Miller et al., 1990). The participant’s score was the number of strings of digits correctly repeated. This score constituted the DIGITS variable for this investigation.

Controlled Oral Word Association Test. (FAS Test; Benton & Hamsher, 1976; Benton et al., 1983). The FAS test is a measure of word fluency or word production. The examinee is given one minute to generate as many words as possible that begin with a specified letter. The letters F, A, and S are most often chosen and will be used for this study. The FAS Test has shown high test-retest reliability ranging from .70 at one year (Snow et al., 1988) to .88 at 19-42 days (desRosiers & Kavanagh, 1987). The FAS Test is well normed and is sensitive in identifying frontal and prefrontal brain damage (Spreen & Strauss, 1991). The dependent variable FAS obtained from this
measure corresponded to the total number of words produced by the participant using all three letters.

**Paced Auditory Serial Addition Test.** (PASAT; Gronwall, 1977). The PASAT has been used to assess sustained attention and concentration, as well as information processing. The test involves auditory presentation to the examinee of a series of digits. The participant adds each presented digit to the preceding one, saying the sum aloud. The PASAT has shown excellent internal consistency with a split-half reliability measure of .96 (Egan, 1988). Spreen and Strauss (1991) have described the PASAT as a "very sensitive test of deficit in mildly brain-injured people," (p.148). Because the test is "quite demanding" even for non-injured subjects (Spreen & Strauss, 1991; p. 148), a shortened version developed and normed by Rao, Leo, Bernardin, and Unverzagt (1991) in which digits are presented at 3 second intervals, then at 2 second intervals was used. The score obtained from this measure (PASATTOT) was the sum of the number of correct responses given on the two trials.

**Procedure**

Following the receipt of informed consent, all participants were administered the WRAT-3 reading test to determine eligibility for the investigation. The participants next completed a short demographic information sheet, and the remaining measures were administered to all subjects in the following order:

1) STAI-S  
2) SILS  
3) RAVLT (free recall portion)  
4) TMT Parts A and B  
5) Block Design  
6) GPT  
7) Digit Span Forward  
8) RAVLT Delay  
9) FAS Test  
10) PASAT

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The testing order was the same for all subjects because their performances were compared against one another, and the study was not intended to examine specific deficits within domains of functioning. Therefore, the effects of order of presentation were not assessed. The STAI-S was administered first in order to obtain a measurement of the subjects' anxiety levels as testing began. Next, the SILS was administered because the score on this test was used as a control variable. The RAVLT was the first neuropsychological measure administered because it contains a built in delay that must be administered later in the session. The TMT parts A and B, Block Design, GPT, and Digit Span followed next in order to fill the time between the RAVLT free recall and delayed recall with non-verbal tests that would not interfere with memory of the word list for the RAVLT. Next, the RAVLT delayed recall test was administered due to the constraint that it must follow the free recall portion by 20 minutes. The FAS test followed in order that the PASAT might be administered last due to the high rate of failure on this test and the increased anxiety and discomfort it can engender. The order of testing was chosen to maximize efficiency, gathering the greatest amount of information in the least amount of time while minimizing subject fatigue.

The 1 - 1.5 hour battery was administered in a single setting. To decrease the likelihood of fatigue, a two minute break was offered after the RAVLT delayed recall was completed. No breaks were given before that point, as the time between initial administration of the RAVLT and the delayed recall test is fixed at 20 minutes. Testing was administered with the examiner sitting across a desk from the subject in a room.
with adequate lighting that was relatively free of distractions. As stated above, after administration of each measure performance appraisals were obtained.

Three examiners were used for this investigation. All examiners were familiar with the administration of psychological measures, and used a standardized instruction sheet which is reproduced in Appendix D.
Results

The sample size for the current study totaled 76 participants, 38 of whom were HIV seropositive, and 38 seronegative individuals. Of the participants, 58 (76.3%) were white, 17 (22.1%) were African-American, and 1 (1.3%) was Native American. For the purposes of the investigation, the latter two groups were combined to yield race categories of white, and non-white. Sixty-two (80.5%) participants were male, and 14 (18.2%) were female. The ages of participants ranged from 19 - 53 years, with a mean age for participants of 34.5 years (SD = 7.4 years). The mean education level was 15.0 (SD = 2.2 years), with a range of 11 - 20 years. The mean age- and sex- corrected STAI-S T-score for all participants was 48.7 (SD = 8.2), indicating that the anxiety level for the sample was in the average range when compared to the normative data for the measure.

Of the 38 participants with HIV disease, 26 (65.8%) were prescribed (and reported taking) one or more anti-retroviral medications (including reverse transcriptase inhibitors as well as protease inhibitors). Twelve (34.2%) reported that they either had not been prescribed medication, or had chosen not to take those that had been prescribed. The mean CD4 count for the HIV seropositive participants was 443.4 CD4/mm$^3$ (SD = 175 CD4/mm$^3$), and ranged from 210 - 982 CD4/mm$^3$. For a listing of demographic information, please see Table 2.

For the first set of analyses, only those subjects whose STAI-S score fell in the highest one third of all scores or the lowest one third of all scores were included in the
Table 2
Demographic Information for the Entire Sample and for Each of the HIV Serostatus Subgroups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Entire Sample</th>
<th>HIV +</th>
<th>HIV -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>58</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td>Non-white</td>
<td>18</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>Female</td>
<td>14</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Age</td>
<td>34.5 yrs.</td>
<td>34.3 yrs.</td>
<td>34.7 yrs.</td>
</tr>
<tr>
<td>Education</td>
<td>15.0 yrs.</td>
<td>14.1 yrs.</td>
<td>15.9 yrs.</td>
</tr>
<tr>
<td>STAI-S T-score</td>
<td>48.7</td>
<td>50.3</td>
<td>47.1</td>
</tr>
<tr>
<td>CD4 count</td>
<td>N/A</td>
<td>443.4 CD4/mm³</td>
<td>N/A</td>
</tr>
<tr>
<td>Medication status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>N/A</td>
<td>26</td>
<td>N/A</td>
</tr>
<tr>
<td>No</td>
<td>N/A</td>
<td>12</td>
<td>N/A</td>
</tr>
</tbody>
</table>

analyses. Therefore, only participants scoring 51 or higher, or 45 or lower on the STA1-S were utilized. When the two groups were further divided according to their HIV serostatus, four groups were created. In order to increase the number of participants included in the analyses, for those participants with missing PASATTOT scores (N = 4), the overall sample average PASATTOT score of 83 for the entire sample was substituted in place of the missing data. The groups were: low anxious - HIV seronegative (N=13), low anxious - HIV seropositive (N=8), high anxious - HIV seronegative (N=11), and high anxious - HIV seropositive (N=17). Chi-squared tests were conducted on these four groups to determine group equality in terms of race and sex, and these were found to be non-significant (for $X^2$ values and significance levels please refer to Table 3).
Table 3
$X^2$ Values Comparing HIV Seropositive and HIV Seronegative Participants at High and Low Anxiety Levels as Determined Using a Tertile Split of Anxiety Scores.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety Level</th>
<th>$X^2$</th>
<th>Significance</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>RACE</td>
<td>Low</td>
<td>0.50</td>
<td>.477</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>3.02</td>
<td>.082</td>
<td>1</td>
</tr>
<tr>
<td>SEX</td>
<td>Low</td>
<td>0.03</td>
<td>.854</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>0.22</td>
<td>.636</td>
<td>1</td>
</tr>
</tbody>
</table>

To determine group equality for the control variables age, education, and Shipley total score, 2 X 2 ANOVA's were performed using the scores on these tests as dependent variables. The groups did not differ significantly in terms of age of participants or Shipley total score. However, ANOVA revealed a main effect for HIV in terms of years of education with the HIV seronegative subjects being more educated (mean = 16.2 years) than those infected with HIV (mean 14.2 years), $F(2,48) = 9.46, p < .01$. Therefore, in subsequent analyses involving these groups, education was entered as a covariate to control for any confounding effects.

Multivariate analysis of covariance (MANCOVA) used to examine group differences on the measures that assess areas that have been shown to be disturbed in patients with HIV revealed no significant two-way interactions, or main effects. While examination of univariate tests does not typically follow a non-significant MANCOVA, for the purposes of this investigation, the univariate results will be reported to highlight areas which may be important to investigate in future endeavors of this nature.

Examination of the univariate tests, revealed a significant two-way interaction for the RAVLT total score ($F(1,43) = 2.33, p < .02$) in which those participants in the high
anxious - HIV seropositive group scored significantly more poorly (mean = 41.2, SD = 7.4) than participants in the low anxious - HIV seropositive group (mean = 51.1, SD = 4.0). Differing anxiety levels led to differences in scores, but only for those participants with HIV. In addition, a main effect was observed for anxiety on the time to complete the Trail Making Test part B (F(1,43) = 4.34, p < .05). Group means indicated that those participants in the high anxiety groups required longer times to complete the measure than patients in the low anxiety group regardless of their HIV serostatus.

A MANCOVA performed on those variables that are frequently disturbed in anxious participants again revealed neither a significant two-way interaction, nor a significant main effect for either anxiety or HIV serostatus. Examination of the univariate tests revealed a significant main effect for anxiety level on the Block Design variable (F(1,44) = 4.06, p = .05). Inspection of the group means indicated that those participants in the high anxiety groups performed more poorly on the measure than those with less anxiety, regardless of their HIV serostatus. For group mean scores on each of the measures administered, please see Table 4.

The next set of analyses utilized scores from all participants. The participants were again divided into four groups depending on their STAI-S scores, and their HIV serostatus, and again the overall sample mean was substituted for all missing PASATTOT scores. For the following analyses, however, a median split at the STAI-S T-score of 48 divided the participants into low and high anxiety groups. The resulting groups were: low anxious - HIV seronegative (N=21), low anxious - HIV seropositive
Table 4
Mean Test Scores (and Standard Deviations) for each Group (as Created Using a Tertile Split of STAI-S Scores and HIV Serostatus) on Dependent Measures.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Lo Anx/HIV-</th>
<th>Hi Anx/HIV-</th>
<th>Lo Anx/HIV+</th>
<th>Hi Anx/HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVLTTOT</td>
<td>47.2 (9.3)</td>
<td>47.5 (4.6)</td>
<td>51.1 (4.0)*</td>
<td>41.2 (7.4)*</td>
</tr>
<tr>
<td>RAVLTDAY</td>
<td>9.4 (3.3)</td>
<td>9.4 (2.9)</td>
<td>10.0 (1.8)</td>
<td>7.2 (3.2)</td>
</tr>
<tr>
<td>FAS</td>
<td>42.7 (12.2)</td>
<td>44.5 (10.7)</td>
<td>44.8 (10.4)</td>
<td>37.6 (9.9)</td>
</tr>
<tr>
<td>GPTD</td>
<td>66.4 (8.5)</td>
<td>64.8 (6.4)</td>
<td>64.0 (12.4)</td>
<td>75.3 (16.0)</td>
</tr>
<tr>
<td>GPTN</td>
<td>71.2 (12.4)</td>
<td>71.7 (11.0)</td>
<td>69.0 (12.4)</td>
<td>81.1 (18.9)</td>
</tr>
<tr>
<td>PASATTOT</td>
<td>83.9 (19.1)</td>
<td>82.9 (22.4)</td>
<td>83.6 (12.5)</td>
<td>75.4 (23.0)</td>
</tr>
<tr>
<td>TMTA</td>
<td>22.7 (6.2)</td>
<td>22.5 (7.2)</td>
<td>23.6 (6.1)</td>
<td>26.0 (8.9)</td>
</tr>
<tr>
<td>TMTB</td>
<td>51.9 (16.4)**</td>
<td>54.4 (20.7)</td>
<td>49.1 (14.0)**</td>
<td>69.9 (20.3)</td>
</tr>
<tr>
<td>BLOCKS</td>
<td>34.5 (10.1)**</td>
<td>32.7 (8.9)</td>
<td>38.2 (7.4)**</td>
<td>26.4 (9.6)</td>
</tr>
<tr>
<td>DIGITS</td>
<td>8.1 (2.7)</td>
<td>9.1 (1.3)</td>
<td>8.4 (2.6)</td>
<td>7.1 (2.3)</td>
</tr>
</tbody>
</table>

Note. Lo Anx/HIV- = Low anxiety - HIV seronegative group; Hi Anx/HIV- = High anxiety - HIV seronegative group; Lo Anx/HIV+ = Low anxiety - HIV seropositive group; Hi Anx/HIV+ = High anxiety - HIV seropositive group.
* = Indicates the two groups significantly different within the significant interaction.
** = Indicates a main effect with the two groups with highest scores marked with (**).

(N=18), high anxious - HIV seronegative (N=17), and high anxious - HIV seropositive (N=20).

Chi-squared tests were performed for these groups on the control variables race and sex were found to be non-significant, indicating that there were no group differences on these variables (see Table 5). The data were then subjected to 2 X 2 ANOVA's for the variables age, education level, and Shipley total score. As before, ANOVA's for age and Shipley total score were not significant, a main effect for HIV was again found with regard to education level ($F(1,75) = 15.00, p < .001$) with the HIV seropositive participants being less educated (mean = 14.11 years) than the HIV seronegative participants (mean = 15.92 years). As with the previous set of analyses,
Table 5
X² Values Comparing HIV Seropositive and HIV Seronegative Participants at High and Low Anxiety Levels as Determined Using a Median Split of Anxiety Scores.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anxiety Level</th>
<th>X²</th>
<th>Significance</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>RACE</td>
<td>Low</td>
<td>1.04</td>
<td>.308</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>1.80</td>
<td>.179</td>
<td>1</td>
</tr>
<tr>
<td>SEX</td>
<td>Low</td>
<td>0.47</td>
<td>.493</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>0.07</td>
<td>.795</td>
<td>1</td>
</tr>
</tbody>
</table>

education was therefore used as a covariate for all analyses using these groups. As with the previous set of analyses, the scores on the measures that are often disturbed in patients with HIV were subjected to a 2 X 2 MANCOVA. Again, the MANCOVA was not significant for the two-way interaction, or for main effects for anxiety or HIV serostatus. Examination of the univariate tests revealed no significant group differences.

Next, a MANCOVA was performed on the scores for the measures thought to be sensitive to differences in anxiety level. This MANCOVA was also non-significant for the two-way interaction as well as for main effects for anxiety and HIV serostatus. Again, the univariate tests were not significant. Group mean scores for each of the variables are listed in Table 6.

Finally, the two HIV groups were compared to determine whether they differed in terms of their anxiety levels. While the ANOVA on these groups did not indicate a significant difference, the difference did approach significance (F(1,75) = 3.00, p < .09). For that reason, the variables most often found to be sensitive to HIV serostatus were entered into a one-way MANCOVA with education and STAI-S scores entered as
Table 6
Mean Test Scores (and Standard Deviations) for each Group (as Created Using a Median Split of STAI-S Scores and HIV Serostatus) on Dependent Measures.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Lo Anx/HIV-</th>
<th>Hi Anx/HIV-</th>
<th>Lo Anx/HIV+</th>
<th>Hi Anx/HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVLTTOT</td>
<td>49.0 (8.8)</td>
<td>49.0 (6.0)</td>
<td>48.6 (8.8)</td>
<td>42.5 (7.5)</td>
</tr>
<tr>
<td>RAVLTDAY</td>
<td>9.8 (2.9)</td>
<td>9.6 (2.9)</td>
<td>9.5 (2.4)</td>
<td>7.6 (3.1)</td>
</tr>
<tr>
<td>FAS</td>
<td>44.0 (12.2)</td>
<td>43.2 (9.2)</td>
<td>42.1 (12.0)</td>
<td>38.9 (10.9)</td>
</tr>
<tr>
<td>GPTD</td>
<td>66.6 (8.4)</td>
<td>65.5 (6.2)</td>
<td>68.5 (14.6)</td>
<td>73.5 (15.5)</td>
</tr>
<tr>
<td>GPTN</td>
<td>71.0 (10.6)</td>
<td>73.5 (12.4)</td>
<td>74.0 (15.8)</td>
<td>80.3 (18.7)</td>
</tr>
<tr>
<td>PASATTOT</td>
<td>89.3 (18.9)</td>
<td>82.0 (20.7)</td>
<td>84.0 (19.4)</td>
<td>75.8 (21.2)</td>
</tr>
<tr>
<td>TMTA</td>
<td>22.4 (6.5)</td>
<td>21.9 (6.6)</td>
<td>24.4 (6.8)</td>
<td>25.0 (8.7)</td>
</tr>
<tr>
<td>TMTB</td>
<td>52.4 (14.1)</td>
<td>53.5 (21.3)</td>
<td>58.7 (31.6)</td>
<td>66.6 (20.2)</td>
</tr>
<tr>
<td>BLOCKS</td>
<td>35.2 (10.2)</td>
<td>34.4 (9.3)</td>
<td>35.2 (11.2)</td>
<td>26.8 (9.8)</td>
</tr>
<tr>
<td>DIGITS</td>
<td>8.7 (2.6)</td>
<td>8.7 (1.6)</td>
<td>8.3 (2.8)</td>
<td>7.4 (2.3)</td>
</tr>
</tbody>
</table>

Note. Lo Anx/HIV- = Low anxiety - HIV seronegative group; Hi Anx/HIV- = High anxiety - HIV seronegative group; Lo Anx/HIV+ = Low anxiety - HIV seropositive group; Hi Anx/HIV+ = High anxiety - HIV seropositive group.

covariates in order to examine differences between the HIV serostatus groups when their anxiety level was held constant. This MANCOVA was also found to be non-significant, as were the univariate follow up tests. For group means on dependent variables for each of the HIV groups, please see Table 7.

The second part of the study used the positive and negative appraisal scores derived from the participants' assessments of their performances. As described above, these scores were computed by asking the participant to rate his or her performance on a scale of below average, average, or above average. These judgments were then compared to their actual performance in relation to all other participants. From these appraisals, two scores were determined, the extent to which the participant underestimated his/her performance (NEGAPP) which was the absolute value of the
Table 7
Mean Test Score (and Standard Deviations) by HIV Serostatus Group on Dependent Measures, Controlling for Anxiety Level.

<table>
<thead>
<tr>
<th>Measure</th>
<th>HIV seropositive</th>
<th>HIV seronegative</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVLTTOT</td>
<td>45.4 (8.6)</td>
<td>49.0 (7.6)</td>
</tr>
<tr>
<td>RAVLTDLAY</td>
<td>8.5 (2.9)</td>
<td>9.7 (2.8)</td>
</tr>
<tr>
<td>FAS</td>
<td>40.5 (11.4)</td>
<td>43.6 (10.8)</td>
</tr>
<tr>
<td>GPTD</td>
<td>71.1 (15.1)</td>
<td>66.1 (7.4)</td>
</tr>
<tr>
<td>GPTN</td>
<td>77.2 (17.4)</td>
<td>72.1 (11.3)</td>
</tr>
<tr>
<td>PASATTOT</td>
<td>79.8 (20.4)</td>
<td>86.1 (19.8)</td>
</tr>
<tr>
<td>TMTA</td>
<td>24.8 (7.7)</td>
<td>22.2 (6.5)</td>
</tr>
<tr>
<td>TMTB</td>
<td>62.8 (26.3)</td>
<td>52.9 (17.5)</td>
</tr>
<tr>
<td>BLOCKS</td>
<td>30.8 (11.2)</td>
<td>34.8 (9.7)</td>
</tr>
<tr>
<td>DIGITS</td>
<td>7.8 (2.5)</td>
<td>8.7 (2.2)</td>
</tr>
</tbody>
</table>

sum of his/her under appraisal scores, and the extent to which the participant overestimated his/her performance (POSAPP) defined as the sum of his or her over appraisal scores.

Two by two ANOVA's were used to determine if the four groups differed in the accuracy of their performance appraisals. The first two ANOVA's were performed on the NEGAPP and POSAPP scores of the groups defined by the tertile split (participants at the extreme anxiety levels). The second set of ANOVA's was conducted to determine if the groups determined by the median split of STAI scores differed significantly on NEGAPP or POSAPP scores. None of the ANOVA's were significant, indicating that neither a participant's HIV serostatus, nor his/her anxiety level was related to his/her ability to accurately judge his/her performance. For NEGAPP and POSAPP scores for these groups please see Tables 8 and 9.
Table 8
Mean appraisals scores per group (as Created Using a Tertile Split of Anxiety Score and HIV Serostatus).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lo Anx/HIV-</th>
<th>Hi Anx/HIV-</th>
<th>Lo Anx/HIV+</th>
<th>Hi Anx/HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEGAPP</td>
<td>2.38</td>
<td>3.00</td>
<td>2.13</td>
<td>1.76</td>
</tr>
<tr>
<td>POSAPP</td>
<td>1.54</td>
<td>1.18</td>
<td>1.13</td>
<td>1.94</td>
</tr>
</tbody>
</table>

Note. Lo Anx/HIV- = Low anxiety - HIV seronegative group; Hi Anx/HIV- = High anxiety - HIV seronegative group; Lo Anx/HIV+ = Low anxiety - HIV seropositive group; Hi Anx/HIV+ = High anxiety - HIV seropositive group.

Table 9
Mean appraisals scores per group (as Created Using a Median Split of Anxiety Score and HIV Serostatus).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lo Anx/HTV-</th>
<th>Hi Anx/HTV-</th>
<th>Lo Anx/HTV+</th>
<th>Hi Anx/HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEGAPP</td>
<td>2.57</td>
<td>3.12</td>
<td>2.22</td>
<td>2.05</td>
</tr>
<tr>
<td>POSAPP</td>
<td>1.71</td>
<td>1.06</td>
<td>1.39</td>
<td>1.65</td>
</tr>
</tbody>
</table>

Note. Lo Anx/HTV- = Low anxiety - HTV seronegative group; Hi Anx/HTV- = High anxiety - HTV seronegative group; Lo Anx/HTV+ = Low anxiety - HIV seropositive group; Hi Anx/HTV+ = High anxiety - HIV seropositive group.

The final analysis was performed to test for medication effects, therefore only scores for those participants with HIV were utilized. The HIV seropositive participants were divided into two groups based on whether they followed a medication regimen (for HIV) or not. In order to increase the number of cases utilized for the analysis, for any participant who did not complete the PASAT (N = 3), the average PASAT total score for HIV seropositive patients (80) was entered as his/her score. A MANOVA comparing scores from participants who reported taking HIV medications with those who did not on variables that are reportedly disturbed in HIV seropositive patients was not significant. Examination of the univariate tests revealed a significant effect for
medication status for the variable GPTD ($F(1,35) = 5.24, p < .03$). Groups means indicated that those participants taking medication were slower to complete the Grooved Pegboard Test than the patients who were not taking medication. These results indicate that for this sample, participants on medication did not perform significantly differently from those who were not. Mean scores on the dependent variables for the medicated and nonmedicated groups are listed in Table 10.

Table 10
Mean Scores (and Standard Deviations) for Each Dependent Variable for Medicated Versus Nonmedicated HIV Seropositive Participants.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Medicated</th>
<th>Nonmedicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVLT TOT</td>
<td>44.1 (9.4)</td>
<td>48.7 (5.4)</td>
</tr>
<tr>
<td>RAVLTDLAY</td>
<td>8.1 (3.0)</td>
<td>9.4 (2.6)</td>
</tr>
<tr>
<td>FAS</td>
<td>38.6 (12.3)</td>
<td>45.0 (7.6)</td>
</tr>
<tr>
<td>GPTD</td>
<td>74.6 (16.0)</td>
<td>62.8 (8.6)</td>
</tr>
<tr>
<td>GPTN</td>
<td>79.7 (19.5)</td>
<td>71.4 (9.7)</td>
</tr>
<tr>
<td>PASAT TOT</td>
<td>77.6 (20.4)</td>
<td>85.4 (18.5)</td>
</tr>
<tr>
<td>TMTA</td>
<td>25.3 (8.7)</td>
<td>23.4 (4.7)</td>
</tr>
<tr>
<td>TMTB</td>
<td>65.7 (29.7)</td>
<td>55.7 (14.3)</td>
</tr>
</tbody>
</table>

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Discussion

Although it would be difficult to find anyone with knowledge in the field to dispute the evidence of brain dysfunction in late stage HIV disease, such findings are much less clear in patients early in the disease process. The literature on neuropsychological functioning in patients with asymptomatic HIV disease is widely discrepant, and opinions on the merits of the investigations published, as well as the validity of the results are divergent. Many prominent researchers have joined the debate on both sides of the issue.

A number of investigations have been published in support of each of the positions, and several theories have been advanced to explain the varied results. Some researchers blame inadequate study design for an inability to find positive results. Others have suggested that many of the tests used are not sensitive enough to detect the subtle deficiencies of which patients with HIV complain. Finally, some investigators have pointed to the notion that areas of deficits differ across individuals, and pooling of test scores leads to the lack of positive findings.

The current study was designed with the intention of ruling out at least one of the possible explanations for differences between HIV seropositive and HIV seronegative individuals on neuropsychological measures. To date, no studies have been published in which possible differing anxiety levels between HIV seropositive and HIV seronegative participants have been addressed. Given the literature that test performance can be affected by extreme anxiety, it seems possible that this variable could influence test performance in patients with HIV. It was the intention of this study

50

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to demonstrate that disturbed performance on neuropsychological tests in HIV seropositive participants could not be accounted for by differing anxiety levels, and was in fact due to differences in HIV serostatus.

In this investigation, the HIV seropositive and seronegative groups did not differ in terms of their performance on the neuropsychological tests administered. Additionally, the anxiety level for the two groups was not significantly different. However, while they did not differ significantly in terms of their level of anxiety, the difference did approach significance. For that reason, their neuropsychological test performance was compared while controlling for any differences that may have been due to anxiety. In fact, any differences between their performance on the neuropsychological measures was even less obvious under these conditions. These results would seem to indicate that on the basis of this investigation, anxiety cannot be ruled out as a contributor to neuropsychological deficits found in previous investigations, but it cannot be identified as a contributor either because the results were unchanged under differing anxiety conditions.

To more thoroughly investigate the possible role of anxiety in contributing to disturbance in neuropsychological functioning in HIV patients, four groups were created based on scores on the STAI-S and the participants' HIV serostatus. It was expected that for those tests that in previous studies had evidenced disturbed performance in HIV patients, a main effect for HIV serostatus would be observed. Additionally, for those tests which have been demonstrated to be sensitive to anxiety level, a main effect for level of anxiety was anticipated. Finding these results would
have indicated that neuropsychological deficits in HIV patients are in fact related to differing serostatus regardless of anxiety level. This claim would have been bolstered by a main effect for anxiety level on the anxiety sensitive tests which would have shown a dissociation between neuropsychological deficits due to HIV and those related to anxiety.

The anticipated results, however, were not realized. When the groups were defined by a median split of scores on the STAI-S, MANCOVA's on both the measures thought to be sensitive to anxiety level and those thought sensitive to HIV serostatus were not significant for the interaction between anxiety level and HIV serostatus, or for main effects. Likewise, when the groups were chosen to maximize the difference between the anxiety levels (by taking the top and bottom tertiles), the same MANCOVA's were again found to be non-significant. The only differences that were found were on individual tests in the groups representing the extreme anxiety levels. The tests on which significant differences were found were the Block Design subtest of the WAIS-R and the Trail Making Test Part B (on which the participants high in anxiety level performed more poorly), and the total number of words recalled on the RAVLT, which highly anxious participants performed more poorly, but only in the HIV seropositive condition. Again, it would seem that from the results obtained in this investigation, anxiety cannot be ruled out as a contributor to differences in neuropsychological test performance between HIV serostatus groups.

The final hypothesis investigated in this study involved the participants' appraisals of their performances. It was thought that those participants who were most
anxious would be more likely to judge their performance to be lower than the actual level, and that this effect would be most pronounced in the HIV seropositive participants. The test of this effect was also found to be non-significant. It is unclear if the assumption was invalid, or if the method of investigation was faulty. For this study, the participants were asked to appraise their performances on the measures given, but, as many complained, they had no frame of reference for the measures because they were unfamiliar with the tests. Perhaps a better strategy which may have been more likely to yield positive results would have been to ask not how they felt about their performance on specific tests, but to estimate their abilities in the areas tested.

The question remains why the anticipated main effects for neuropsychological performance were not found in this investigation, and what could be changed in future research efforts to more accurately examine this population. One problem that likely plagued this research as it does many other projects was the influence of selection bias. It is impossible to determine to what extent the data collected were influenced by differences in those people who volunteered to participate, versus those who refused. It is very likely that those patients who felt that they had begun to experience cognitive losses may have been more reluctant to have this suspicion confirmed, and still others may have been less willing to participate due to extreme anxiety invoked by the testing situation. In fact, these were the explanations offered by several clinic patients who chose not to participate. Ironically, the inclusion of these people would very likely have strengthened this investigation.
Additionally, one might argue that the number of participants in this investigation was inadequate to provide significant results. Although this criticism is valid, and observed power levels were low, it is important to note that when the F values and significance levels for the MANCOVA's were examined, the F values were found to be very small, and the probability levels very high. These statistics indicate that while the group means were in the predicted directions, the effect size for the effects under investigation were sufficiently small that even if enough subjects had been recruited to find significance with adequate power, the results would not have been any more meaningful in terms of clinical relevance.

One of the requirements for participation in this project was the ability to read at a sixth grade level. For that reason, several potential participants were excluded from this study, and others refused to participate when they realized that their reading level would be assessed. Given the data that differences in neuropsychological test performance between HIV seropositive and HIV seronegative participants are most often seen in less educated patients, the exclusion of this group was a shortcoming of this investigation. The lack of positive results in this investigation seems to support previous findings of a protective effect for higher education levels against cognitive loss (Motimer & Graves, 1993; Stern, et al., 1994; Zhang, et al., 1990).

Finally, the majority of the HIV seropositive participants in this investigation reported following a regimen of anti-viral medication. Additionally, because the HOP Clinic at Medical Center of Louisiana is an AIDS Clinical Trials Unit, of those on medication, all but two had been prescribed protease inhibitors, the newest class of
anti-retroviral medication. Because of the novelty of these drugs, they have not received the investigative attention of older medications. It is known that these medications, alone and, more frequently, in combination with reverse transcriptase inhibitors, can drop the level of viral RNA copies (viral load) in a patient's blood to undetectable levels (Cohen, 1996; Deeks, Smith, Holodniy, & Kahn, 1997). While this has been associated with improved physical functioning and longer survival time (Cohen, 1996, Deeks et al., 1997), it remains to be seen if this improvement translates into improved cognitive functioning as well (although this is likely given the documented improvement in cognitive function associated with other anti-retroviral medication (Portegies et al., 1993; Portegies et al., 1989; Schmitt et al., 1998; Sidtis et al., 1993)). Given that the MANOVA comparing those participants taking medication to those participants who were not was nonsignificant, it is impossible to point to either a positive or negative effect for medication in the HIV seropositive participants. However, when group mean scores were considered, the mean scores for all measures for the medication groups were lower (though not significantly) than their nonmedicated counterparts. A possible explanation for this unexpected finding is that the subjects on medication were the least healthy (while viral load estimates were not available, the mean CD4 count of the medication groups was lower than that of the nonmedicated group, though not significantly) and they therefore did not perform as well as the nonmedicated group. Also, given the lack of research on the protease inhibitors, it is possible that they could in some way have adversely affected the performance of these participants due to an unreported toxic side-effect of the medication.
Given the criticisms outlined above, several suggestions present themselves as ways to improve upon the design of the study. If the study had been funded by an outside agency, it would be possible to pay potential subjects, which would likely increase participation. The desire for monetary compensation was voiced most often by female clinic patients, although it was a consideration for many other potential participants regardless of their gender. If the investigator were able to pay the participants, the question of selection bias would not have been removed, but it more than likely would have been lessened, and a greater number of participants might have been recruited leading to a wider range of anxiety levels as well as cognitive abilities.

Finally, any investigation of this type must control for medication effects. As protease inhibitors become more widely available, their potential effects on cognitive functioning will be better described. With this knowledge, investigators will be better able to design their research projects to take into account these effects.

The results of this investigation failed to rule out the possibility that anxiety may contribute to deficits in cognitive functioning in HIV seropositive patients, nor did it confirm this possibility. Although the stated goal of the project was to rule out a role for anxiety, it is important to note that regardless of the reason for these deficits, many patients continue to complain of subtle changes in their cognitive abilities, and these complaints should be taken seriously. This investigation does, however, point to specific improvements that can be made for future research endeavors, and highlights a need for further investigation, especially in the area of medication effects of the newer classes of anti-retroviral medication.
References


57


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Appendix A

CDC (1992) Category A Conditions

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute primary HIV infection with accompanying illness or history of acute HIV infection
Appendix B

CDC (1992) Category B Symptoms: Attributed to or Requiring Management Complicated by HIV

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting more than one month
- Hairy leukoplakia, oral
- Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome
- Idiopathic thrombocytopenic purpura
- Listeriosis
- Pelvic inflammatory disease, particularly if complicated tubo-ovarian abscess
- Peripheral neuropathy
Appendix C

Conditions Included in the 1993 AIDS Surveillance Case Definition (CDC, 1992)

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (> 1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV - related
- Herpes simplex: chronic ulcer(s) (> 1 month's duration); or bronchitis, Pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (> 1 month's duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis, any site (pulmonary or extrapulmonary)
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis carinii* pneumonia
- Pneumonia, recurrent
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV
Appendix D

Instructions to Examiners

Words in all capital letters are spoken by the examiner. Please remember to obtain a performance appraisal after each of the dependent variables (refer to Performance Appraisal Sheet for instructions).

1. **Wide Range Achievement Test Reading** - Present the reading list to the subject and say: LOOK AT EACH OF THESE WORDS CAREFULLY (point). READ THE WORDS ACROSS THE PAGE SO I CAN HEAR YOU. WHEN YOU FINISH THE FIRST LINE, GO TO THE NEXT LINE AND SO ON. Allow 10 seconds for the subject to respond. If he/she is in the middle of a response allow him/her to continue. If there is no response, say: TRY THE NEXT ONE PLEASE. After the first error, the individual should be asked to repeat the word which was missed. If the word is said correctly, score as correct. No other help should be given. Do not ask the subject to repeat any other words unless you could not hear the subject. In that case say: I COULD NOT HEAR YOU CLEARLY. PLEASE SAY THE WORD AGAIN JUST AS YOU DID THE FIRST TIME. For this study, the subjects need only correctly read 22 words before missing 10 in a row. If they miss 10 in a row before correctly reading 22 they may not be included in the sample. Do not count off if the person has poor diction, or if the error can be attributed to his/her dialect. Circle the number before each item pronounced correctly, and draw a line through the first letter of each word pronounced incorrectly.
2. **CES-D** - CIRCLE THE NUMBER FOR EACH STATEMENT WHICH BEST DESCRIBES HOW OFTEN YOU FELT THIS WAY **DURING THE PAST WEEK**.

3. **Self-Evaluation Questionnaire (State)** - A NUMBER OF STATEMENTS THAT PEOPLE HAVE USED TO DESCRIBE HOW THEY FEEL ARE GIVEN BELOW. READ THE STATEMENTS BELOW AND INDICATE HOW YOU FEEL **AT THE MOMENT** BY CIRCLING THE APPROPRIATE NUMBER.

4. **Shipley Institute of Living Scale - Part I** IN THE TEST BELOW, THE FIRST WORD IN EACH LINE IS PRINTED IN CAPITAL LETTERS. OPPOSITE IT ARE FOUR OTHER WORDS. CIRCLE THE **ONE WORD** WHICH MEANS THE **SAME THING**, OR NEARLY THE SAME THING AS THE FIRST WORD. IF YOU DON'T KNOW, GUESS. BE SURE TO CIRCLE THE **ONE WORD** IN EACH LINE THAT MEANS THE SAME THING AS THE FIRST WORD. The subject is given ten minutes or until he/she indicates that he/she is finished to complete Part I. **Part II** COMPLETE THE FOLLOWING BY FILLING IN EITHER A NUMBER OF A LETTER FOR EACH DASH. DO THE ITEMS IN ORDER, BUT DON'T SPEND TOO MUCH TIME ON ANY ONE ITEM. Again the subject is given ten minutes or until he/she indicates that he/she is finished.

5. **Rey Auditory Verbal Learning Test** - I AM GOING TO READ A LIST OF WORDS. LISTEN CAREFULLY, FOR WHEN I STOP YOU ARE TO REPEAT BACK AS
MANY WORDS AS YOU CAN REMEMBER. IT DOESN'T MATTER WHAT
ORDER YOU REPEAT THEM. JUST TRY TO REMEMBER AS MANY AS YOU
CAN. Read List A1 aloud, with a one second interval between each word. Use numbers
to keep track of the participant's pattern of recall. No feedback should be given. When
the participant indicates that he/she can recall no more words, the examiner rereads the
list after giving the following set of instructions. NOW I'M GOING TO READ THE
SAME WORDS AGAIN, AND ONCE AGAIN WHEN I STOP I WANT YOU TO
TELL ME AS MANY WORDS AS YOU CAN REMEMBER, INCLUDING THE
WORDS YOU SAID THE FIRST TIME. IT DOESN'T MATTER IN WHAT ORDER
YOU SAY THEM. JUST SAY AS MANY WORDS AS YOU CAN REMEMBER,
WHETHER OR NOT YOU SAID THEM BEFORE. The list is reread for Trials A3
through A5 using Trial A2 instructions each time. After trial A5, the examiner reads
List B with instructions as on the first A trial: NOW I'M GOING TO READ A
SECOND LIST OF WORDS. THIS TIME, YOU ARE TO SAY BACK AS MANY
WORDS OF THIS SECOND LIST AS YOU CAN REMEMBER. THE ORDER IN
WHICH YOU SAY THESE WORDS DOES NOT MATTER. JUST TRY TO
REMEMBER AS MANY AS YOU CAN. Immediately after recall B1, as for recall of
the first list (Trial A6) without further presentation of those words: NOW TELL ME AS
MANY WORDS FROM THE FIRST LIST AS YOU CAN REMEMBER. After a
twentyminute delay period filed with other activity, as the patient to recall the words
from list A (Trial A7): NOW TELL ME AS MANY WORDS FROM THE FIRST LIST
AS YOU CAN REMEMBER.
6. **Trail Making Test (Part A)** - Place the Part A sample sheet on the table directly in front of the subject six inches from the edge of the table. Give subject the pencil and say: **ON THIS PAGE (point) ARE SOME NUMBERS. BEGIN AT THE NUMBER 1 (point to 1) AND DRAW A LINE FROM 1 TO 2 (point to 2), 2 TO 3 (point to 3), 3 TO 4 (point to 4), AND SO ON, IN ORDER UNTIL YOU REACH THE END (point to the circle marked "end"). DRAW THE LINES AS FAST AS YOU CAN. READY! BEGIN!**

If the subject completes the sample items correctly, and in manner which shows that he/she knows what to do, say: **GOOD! LET'S TRY THE NEXT ONE.** Give Part A of the test following the instructions below.

If the subject makes a mistake on Sample A, point out the error and explain it. The following explanations of mistakes serve as illustrations.

A. **YOU STARTED WITH THE WRONG CIRCLE. THIS IS WHERE YOU START (point to the number 1).**

B. **YOU SKIPPED THIS CIRCLE (point to the circle omitted). YOU SHOULD GO FROM NUMBER 1 (point), TO 2 (point), 2 TO 3 (point), AND SO ON, UNTIL YOU REACH THE CIRCLE MARKED END (point).** If it is clear that the subject intended to touch the circle but missed it, do not count it as an omission, but caution the subject to touch the circles.

If the subject still cannot complete the sample, take his/her hand and guide the pencil (eraser end down) through the trail. Then say: **NOW YOU TRY IT.** Return the pencil to the subject and say: **REMEMBER, BEGIN AT NUMBER 1 (point) AND DRAW A LINE FROM 1 TO 2 (point to 2), 2 TO 3 (point to 3), 3 TO 4 (point to 4),**
AND SO ON IN ORDER, UNTIL YOU REACH THE CIRCLE MARKED END (point). DO NOT SKIP AROUND, BUT GO FROM ONE NUMBER TO THE NEXT IN THE PROPER ORDER. REMEMBER TO WORK AS FAST AS YOU CAN.

READY! BEGIN! If the subject succeeds this time, go on to Part A. If not, repeat the procedure until he/she does or until it is evident that he/she cannot.

Test Instructions. ON THIS PAGE ARE NUMBERS FROM 1 TO 25. DO THIS THE SAME WAY. BEGIN AT NUMBER 1 (point) AND DRAW A LINE FROM 1 TO 2 (point to 2), 2 TO 3 (point to 3), 3 TO 4 (point to 4) AND SO ON, IN ORDER, UNTIL YOU REACH THE END (point to 25). REMEMBER, WORK AS FAST AS YOU CAN. READY! BEGIN! Start timing and do not stop. Watch the subject closely and correct any errors immediately by having the subject proceed from the point the mistake occurred. Record the time to complete the test.

7. Trail Making Test (Part B) - NOW WE'LL TRY ANOTHER ONE. Place Sample B in front of the participant and say: ON THIS PAGE ARE SOME NUMBERS AND LETTERS. BEGIN AT NUMBER 1 (point) AND DRAW A LINE FROM 1 TO A (point to A), A TO 2 (point to 2), 2 TO B (point to B), B TO 3 (point to 3), 3 TO C (point to C), AND SO ON, IN ORDER UNTIL YOU REACH THE END (point to the circle marked "end"). REMEMBER, FIRST YOU HAVE A NUMBER (point to 1), THEN A LETTER (point to A), THEN A NUMBER (point to 2), THEN A LETTER (point to B), AND SO ON. DRAW THE LINES AS FAST AS YOU CAN. READY!
BEGIN! If the subject completes the sample correctly, say: GOOD. LET'S TRY THE NEXT ONE. Administer the test with the instructions below.

If the subject makes a mistake, point it out and explain it similarly to the explanations for mistakes for part A. If the subject still cannot complete the sample, guide his/her hand as before. Then repeat the instructions and encourage the subject to try again. If the subject succeeds, proceed to the test, if not, continue to explain it until he/she does succeed, or until it becomes obvious that he/she cannot.

Test Instructions: ON THIS PAGE ARE NUMBERS AND LETTERS. DO THIS THE SAME WAY. BEGIN AT NUMBER 1 (point), AND DRAW A LINE FROM 1 TO A (point to A), A TO 2 (point to 2), 2 TO B (point to B), B TO 3 (point to 3), 3 TO C (point to C), AND SO ON, IN ORDER, UNTIL YOU REACH THE END (point to the circle marked "end"). REMEMBER, FIRST YOU HAVE A NUMBER (point to 1), THEN A LETTER (point to A), THEN A NUMBER (point to 2), THEN A LETTER (point to B), AND SO ON. DON NOT SKIP AROUND, BUT GO FROM ONE CIRCLE TO THE NEXT IN PROPER ORDER. DRAW THE LINES AS FAST AS YOU CAN. READY! BEGIN! Start timing and do not stop. If the subject makes an error, call it to the subject's attention immediately and have him/her proceed from the point the mistake occurred. Record the time to complete the test.

8. Block Design - Place four blocks in view of the subject and say: YOU SEE THESE BLOCKS? THEY ARE ALL ALIKE. ON SOME SIDES THEY ARE ALL RED; ON SOME, ALL WHITE; AND ON SOME, HALF RED AND HALF WHITE. Hold up one
block and turn it to show each side. Then say: I'M GOING TO PUT THEM TOGETHER TO MAKE A DESIGN, WATCH ME. Arrange the four blocks slowly into the design shown on card 1, without exposing the card to the subject. Then, leaving the model intact, give four other blocks to the subject and say: NOW MAKE ONE JUST LIKE THIS. Start timing. Allow 60 seconds. If the subject successfully completes the design within the time limit, proceed to Design 2. If the subject fails, say: WATCH ME AGAIN. Demonstrate again using the subject's blocks. Then scramble the subject's blocks and say: NOW YOU TRY IT AGAIN AND BE SURE TO MAKE IT JUST LIKE MINE. Start timing again and allow 60 seconds. Regardless of performance, proceed to design 2. If the subject attempts to match the examiner's design exactly (all sides) tell him/her that only the top needs to be duplicated.

Design 2 Scramble the subject's blocks. Remove the blocks that served as the model for design 1 and put in their place the card marked (2). Say: THIS TIME WE ARE GOING TO PUT THE BLOCKS TOGETHER TO MAKE THEM LOOK LIKE THIS PICTURE. Point to the card, then say: WATCH ME FIRST. Construct the design slowly, then say: YOU SEE THE TOPS OF THESE BLOCKS LOOK THE SAME AS THIS PICTURE. Scramble the blocks used in the demonstration and say: NOW LOOK AT THE PICTURE AND MAKE ONE JUST LIKE IT WITH THESE BLOCKS. GO AHEAD. Allow 60 seconds. If the subject successfully completes the design, proceed to Design 3. If the subject fails, scramble the blocks and say: WATCH ME AGAIN. Make the design again, then scramble it and say: NOW TRY IT AGAIN. Allow 60 seconds. Regardless of performance, continue to Design 3.
Design 3-9 Scramble the blocks and put out the card marked (3). Say: NOW MAKE ONE LIKE THIS. TRY TO WORK AS QUICKLY AS YOU CAN. TELL ME WHEN YOU HAVE FINISHED. Start timing and allow 60 seconds. When the subject has completed the design or time is up, scramble the block and continue with the next design using the same instructions, or a shortened version once the subject understands the task. For Design 6 say: NOW MAKE ONE LIKE THIS USING NINE BLOCKS. BE SURE TO TELL ME WHEN YOU HAVE FINISHED. For Design 9, do not permit the subject to rotate the card. Continue the test until the subject has failed 3 consecutive trials. A two-trial design is considered failed only if both trials are failed.

9. Grooved Pegboard Test - THIS IS A PEGBOARD, AND THESE ARE PEGS. Point to each, then pick up one of the pegs. ALL OF THE PEGS ARE THE SAME. THEY HAVE A GROOVE. THAT IS, A ROUND SIDE, AND A SQUARE SIDE, AND SO DO THE HOLES IN THE BOARD. WHAT YOU MUST DO IS MATCH THE GROOVE OF THE PEG WITH THE GROOVE OF THE BOARD AND PUT THSES PEGS INTO THE HOLES LIKE THIS. Demonstrate by filling the top row, then take them out again. WHEN I SAY GO, BEGIN HERE AND PUT THE PEGS INTO THE BOARD AS FAST AS YOU CAN USING ONLY YOUR (DOMINANT) HAND. FILL THE TOP ROW COMPLETELY FROM THIS SIDE TO THIS SIDE (demonstrate left to right when using right hand, and right to left when using left hand). DO NOT SKIP ANY. FILL EACH ROW THE SAME WAY YOU FILLED THE TOP ROW. ANY
QUESTIONS? READY, AS FAST AS YOU CAN GO. Begin timing and stop when last peg is in its hole.

10. **Digit Span Forward** - I'M GOING TO SAY SOME NUMBERS. LISTEN CAREFULLY, AND WHEN I AM THROUGH SAY THEM RIGHT AFTER ME. The digits should be given at the rate of one per second. Let the pitch of voice drop on the last digit of each trial. Administer **both** trials of each item, even if the subject passes trial 1. Discontinue after failure on **both** trials of any item. Give 2 points if the subject passes both trials, 1 point if the subject passes only 1, and 0 points if the subject fails both trials.

11. **Remember to give the RAVLT delay.**

12. **F-A-S Test** - Ignore the instructions at the top of the page. I WANT YOU TO NAME AS MANY WORDS AS YOU CAN THAT BEGIN WITH THE LETTER OF THE ALPHABET THAT I WILL GIVE YOU. THERE ARE TWO RULES. FIRST, YOU CANNOT USE DIFFERENT FORMS OF THE SAME WORD. FOR EXAMPLE, IF I GAVE YOU (G), YOU COULD SAY GO, BUT YOU COULD NOT THEN SAY GOES OR GONE. SECOND, YOU CANNOT USE PROPER NAMES, FOR EXAMPLE THE NAME OF A PERSON OR A CITY. NOW HOW MANY WORDS CAN YOU THINK OF THAT BEGIN WITH THE LETTER ___. Allow 60
seconds, and write down all of the words that the subject says in the proper column depending on the time that he/she says the word. Do not administer animals.

13. Paced Auditory Serial Addition Test - I AM GOING TO ASK TO ADD TOGETHER PAIRS OF SINGLE-DIGIT NUMBERS. YOU WILL HEAR A TAPE-RECORDED LIST OF NUMBERS READ ONE AFTER ANOTHER. I WILL ASK YOU TO ADD THE NUMBERS IN PAIRS AND GIVE YOU ANSWERS OUT LOUD. ALTHOUGH THIS IS REALLY A CONCENTRATION TASK, AND NOT A TEST TO SEE HOW WELL YOU CAN ADD, IT MIGHT TO DO A LITTLE ADDING BEFORE I EXPLAIN THE TASK IN MORE DETAIL. PLEASE ADD THE FOLLOWING PAIRS OF NUMBERS TOGETHER AS FAST AS YOU CAN, AND GIVE YOUR ANSWERS OUT LOUD: 3,8 (11); 4,9 (13); 7,8(15); 8,6(14); 8,9(17); 5,7(12); 6,5(11); 6,9(15); 4,7(11); 7,6(13). GOOD. If subject cannot add these numbers, do not administer the test. THE TASK THAT I WANT YOU TO DO INVOLVES ADDING TOGETHER PAIRS OF NUMBERS JUST AS YOU HAVE DONE, EXCEPT THE NUMBERS WILL BE READ AS A LIST ONE AFTER THE OTHER. LET ME GIVE YOU AN EXAMPLE WITH A SHORT, EASY LIST. SUPPOSE I GAVE YOU THE FOLLOWING: 1,2,3,4. HERE'S WHAT YOU WOULD DO. AFTER HEARING THE FIRST TWO NUMBERS ON THE LIST WHICH WERE 1,2, YOU WOULD ADD THESE TOGETHER AND GIVE YOUR ANSWER, 3, 1 + 2 = 3. THE NEXT NUMBER ON THE LIST IS 3, SO WHEN YOU HEARD IT, YOU WOULD ADD THIS NUMBER TO THE NUMBER RIGHT BEFORE IT ON THE LIST.
WHICH WAS 2, AND YOU WOULD GIVE YOUR ANSWER 5, 2 + 3 = 5. ARE YOU FOLLOWING SO FAR? THE LAST NUMBER YOU HEARD WAS 4 (REMEMBER THE LIST WAS 1,2,3,4), SO YOU WOULD ADD 4 TO THE NUMBER RIGHT BEFORE IT WHICH WAS 3, AND GIVE YOUR ANSWER 7, 3 + 4 = 7. THE IMPORTANT THING TO REMEMBER IS THAT YOU MUST ADD EACH NUMBER ON THE LIST TO THE NUMBER BEFORE IT ON THE LIST, AND NOT TO THE ANSWER YOU HAVE JUST GIVEN. YOU CAN FORGET YOUR ANSWERS AS SOON AS YOU HAVE SAID THEM. ALL YOU HAVE TO REMEMBER IS THE LAST DIGIT THAT YOU HEARD AND ADD IT TO THE NEXT DIGIT THAT YOU HEAR. O.K.? LET'S TRY A SHORT LIST AGAIN, ONLY THIS TIME YOU SAY THE ANSWERS. READY? 1,2 (3); 3 (5); 4 (7); NOW LET'S TRY ANOTHER, LONGER PRACTICE LIST OF NUMBERS, THIS TIME THE NUMBERS ON THE LIST WILL NOT BE IN ANY PARTICULAR ORDER.

READY? 4,6 (10); 1 (7); 8 (9); 8 (16); 4 (12); 3 (7); 8 (11); 2 (10); 7 (9). GOOD.

If the subject has difficult understanding the oral directions, then provide a written demonstration. THAT SOUNDS COMPLICATED, LET ME SHOW YOU WHAT I MEAN. Write down a list of numbers (5,3,7,4,2) YOU SEE, YOU ADD THE 5 AND THE 3 TOGETHER AND SAY 8. THEN YOU HAVE TO FORGET THE 8 AND REMEMBER THE 3. WHEN THE 7 COMES ALONG, YOU ADD IT TO THE 3, AND SAY 10. NOW YOU HAVE TO REMEMBER THE 7. ALLRIGHT. WHAT DO YOU SAY AFTER 4? Continue until the subject understands what to do. Say:
IT'S VERY EASY WHEN ALL THE NUMBERS ARE WRITTEN DOWN FOR YOU. TRY IT WITH ME SAYING SOME NUMBERS TO YOU. Say some more.


YOU SEE WHAT I MEAN ABOUT THE TASK MEASURING HOW WELL YOU CAN CONCENTRATE. IT DOESN'T HAVE ANYTHING TO DO WITH HOW SMART YOU ARE. NOW WE'LL TRY THE FIRST REAL TRIAL. THIS TRIAL IS JUST THE SAME AS THE PRACTICE TRIAL YOU'VE JUST DONE, EXCEPT THAT IT IS SIX TIMES AS LONG, SO IT GOES ON FOR ABOUT THREE MINUTES. DON'T WORRY IF YOU MAKE ADDING MISTAKES, OR MISS SOME ANSWERS. THIS IS A DIFFICULT TASK. I WANT TO SEE NOT ONLY HOW LONG YOU CAN KEEP GOING WITHOUT STOPPING, BUT ALSO HOW QUICKLY YOU CAN PICK UP AGAIN IF YOU DO STOP. NO ONE IS EXPECTED TO GET ALL THE ANSWERS. AFTER THIS TRIAL WE WILL TAKE A BREAK AND THEN DO ANOTHER TRIAL AT A FASTER SPEED. Follow along with subject writing the subject’s responses in the blanks provided.
Vita

Joseph Prejean is 29 year old native of Louisiana. He completed his undergraduate studies in 1990 at Washington University in St. Louis where he graduated with honors in Psychology. He continued to pursue his education in Psychology at Louisiana State University where he obtained an master of arts degree in 1993.

After completion of his master’s degree he specialized in clinical neuropsychology, specifically focusing on neuropsychological aspects of the HIV disease spectrum. This interest was further cultivated during his clinical psychology predoctoral internship at the New Orleans Veterans’ Affairs Medical Center.

Following the completion of his doctoral dissertation and graduation in December he will relocate to Atlanta, Georgia where he will pursue further training in therapy and crisis intervention with HIV seropositive patients at Emory University Medical Center.
DOCTORAL EXAMINATION AND DISSERTATION REPORT

Candidate: Joseph Gerald Prejean, Jr.

Major Field: Psychology

Title of Dissertation: The Role of Anxiety in Neuropsychological Dysfunction in Early HIV Disease

Approved:

[Signatures]

Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

[Signatures]

Sarah Pierce

Date of Examination:

September 5, 1997