Subtle Cognitive Decrements And Psychological Distress In Men With Asymptomatic Human Immunodeficiency Virus (HIV) Infection

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Elizabeth Suzanne Stroup
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[redacted]

Kimberly Kerns, Ph.D., Co-supervisor (Department of Psychology)

[redacted]

Pam Duncan, Ph.D., Co-supervisor (Departments of Psychology and Sociology)

[redacted]

Catherine Mateer, Ph.D., Departmental Member (Department of Psychology)

[redacted]

Don Knowles, Ph.D., Outside Member (Department of Psychological Foundations)

[redacted]

Holly Devor, Ph.D., External Examiner (Department of Sociology)

Supervisors: Dr. Kimberly Kerns and Dr. Pam Duncan

Abstract

The presence of subtle neuropsychological decrements (primarily in verbal memory and psychomotor speed) associated with asymptomatic HIV infection has been documented in recent literature. As of yet, the mechanism or mechanisms responsible for these subtle deficits remains unclear. This paper examines the relationship between psychological distress and neuropsychological functioning in 140 asymptomatic HIV+ subjects and 82 HIV- controls. A factor analysis on results of a comprehensive neuropsychological test battery administered to all participants identified five factors. These factors were interpreted to reflect a participant's ability in physical reaction time, attention/speed of processing, verbal memory, motor speed/attention, and executive function. Results of multiple regression analyses indicated that differences in education level between groups accounted for a significant proportion of the variance in several cognitive domains, including reaction time, attention/speed of processing, verbal memory, and executive function. After accounting for education, psychological distress (as measured by the Symptom Checklist-90-Revised) was entered into the multiple regression equation, and was found to account for additional variance on measures of executive function and, to a lesser extent, attention/speed of processing. The last step of multiple regression in which group status was entered revealed that a significant portion of the variance on motor speed/attention was accounted for by group membership. In sum, differences

between HIV+ and HIV- groups on measures of executive function and attention/speed of processing were mediated by psychological distress. Asymptomatic HIV+ subjects experienced greater levels of subjective distress, and performed more poorly on tasks requiring problem solving and the ability to concentrate and think quickly. These findings have implications for early intervention in HIV infection, which might reduce potentially disruptive psychological distress. Decrements on tests of motor speed in the HIV+ group were primarily due to HIV status. Possible explanations for this finding are suggested.

Examiners:

[redacted]

Kimberly Kerns, Ph.D., Co-supervisor (Department of Psychology)

[redacted]

Pam Duncan, Ph.D., Co-supervisor (Departments of Psychology and Sociology)

[redacted]

Catherine Mateer, Ph.D., Departmental Member (Department of Psychology)

[redacted]

Don Knowles, Ph.D., Outside Member (Department of Psychological Foundations)

[redacted]

Holly Devor, Ph.D., External Examiner (Department of Sociology)

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Subtle Cognitive Decrements and Psychological Distress in Men With Asymptomatic Human Immunodeficiency Virus (HIV) Infection

Human Immunodeficiency Virus (HIV), and its sequelae - Acquired Immune Deficiency Syndrome (AIDS) - are among the most formidable infectious syndromes for which a cure, and at very least management, is currently being sought. Not only does HIV infection affect the physical well-being of previously healthy individuals, but in later stages of infection can also result in debilitating cognitive and emotional deficits, such as the AIDS Dementia Complex (ADC) (Price et al., 1988; Price & Brew, 1988). Markers which might be predictive of future cognitive decline have been sought, as well as treatment to combat these frequent outcomes. It has been suggested that neuropsychological testing might reveal subtle cognitive deficits that would be predictive of future declines, but research has produced inconsistent findings.

Asymptomatic HIV Infection and Cognitive Performance

Research in the field of HIV has recently examined the presence of neurocognitive deficits at the asymptomatic stage of illness. In general, findings thus far suggest that 10% to 30% of patients with no symptoms of AIDS (other than generalized lymphadenopathy) experience subtle cognitive impairments which can be detected with existing neuropsychological measures. Subtle cognitive deficits can be defined as small, yet statistically significant, decrements in performance on tests designed to measure cognitive functioning. These deficits may or may not be considered "clinically relevant" (i.e., affecting everyday functioning) depending upon

a researcher's definition of "relevant" and the particular cognitive domain in which the deficit is seen. Numerous studies have reported subtle deficits in areas of cognitive functioning such as verbal memory, attention and concentration, processing speed, reaction times, and psychomotor speed (Bornstein et al., 1992; Bornstein, Nasrallah, Para, Whitacre, Rosenberger, et al., 1993; Lunn et al., 1991). A specific group of deficits commonly reported together (Lunn et al., 1991) involving verbal memory and psychomotor speed have been described. These researchers reported cognitive dysfunction in 35% of their sample of asymptomatic HIV-seropositive (HIV+) subjects, while only 20% HIV-seronegative (HIV-) subjects were classified as impaired. Specifically, deficits were noted on neuropsychological measures of verbal memory and psychomotor speed in the asymptomatic HIV+ group. Sinforiani et al. (1991) also reported decrements on tasks of verbal memory in their asymptomatic HIV+ patients, as did Wilkie, Eisdorfer, Morgan, Loewenstein, and Szapocznik (1990). In a study with rigorous exclusion criteria, R. Stern et al. (1992) found asymptomatic subjects to show worse performance on many neuropsychological tests. However, when education was used as a covariate, differences remained only on tests of motor function.

Deficits in attention and speed of processing have also been described in the literature. Clifford, Jacoby, Miller, Seyfried, and Glicksman (1990) found a consistent, though not statistically significant, trend toward decreased cognitive performance in asymptomatic HIV+ subjects, especially on measures of attention and speed of processing. However, this study had a small number of subjects, few

neuropsychological measures, and no exclusion criteria for subjects. In addition to the previously mentioned verbal memory impairments, Wilkie et al. (1990) also reported general slowing in the performance of asymptomatic HIV+ patients when they were required to manipulate information mentally. In a study using strict exclusion criteria, evidence of decreased neuropsychological performance on a range of cognitive measures was noted in an asymptomatic HIV+ group as compared to a well-matched HIV- cohort (Perry, Belsky-Barr, Barr, & Jacobsberg, 1989). The differences between groups were quite subtle yet consistent, and were observed across several cognitive domains rather than in only one or two specific areas. Using tests tapping a range of cognitive functions, Grant et al. (1987) found a significant trend towards increased impairment with disease progression (asymptomatic HIV+ to AIDS-Related Complex (ARC) to AIDS), although once again this study was limited by its small sample size. One study reporting subtle differences between a mixed group of HIV+ and HIV- homosexual and bisexual men on measures of memory, executive function, attention, and abstract reasoning found these decrements to be robust even when comparing only the asymptomatic HIV+ men with HIV- men (Y. Stern et al., 1991). In a follow-up study, this same cohort of asymptomatic HIV+ males showed significantly more decline in cognitive performance than did their HIV- comparison group (Y. Stern, Sano, Hoover, & Elkin, 1993).

Krikorian, Wrobel, Meinecke, Liang, and Kay (1990) and Krikorian and Wrobel (1991) found increasing deficit across HIV-seronegative (HIV-), asymptomatic HIV+, AIDS-Related Complex (ARC), and AIDS subjects in the areas of attention and

executive functioning. In the latter study, these researchers proposed that the memory deficits reported in other studies may be a manifestation of underlying attentional difficulties similar to the deficits they noted. In other words, memory consolidation and storage may be intact, but impaired subjects may have difficulty acquiring and subsequently retrieving to-be-remembered information. Gibbs, Andrewes, Szmuckler, Mulhall, and Bowden (1990) also suggested this as a possible explanation for poorer memory performance in ARC patients. Slowed reaction times have also been associated with HIV infection (Martin, Heyes, Salazar, Law, & Williams, 1993). Perdices and Cooper (1989) demonstrated a significant trend toward increasing impairment on reaction time measures with disease progression.

Other researchers examining this issue have failed to find the proposed deficits (Gibbs et al., 1990; Janssen et al., 1989; Klusman, Moulton, Hornbostel, Picano, & Beattie, 1991; Swanson, Kessler, Cronin-Stubbs, Bieliauskas, & Zeller, 1991). McAllister et al. (1992) found no significant difference between asymptomatic HIV+ and HIV- subjects when they compared the two on neuropsychological measures. However, when subjects were classified as impaired or not impaired (with impairment defined as performance on at least one neuropsychological measure at least two standard deviations below the mean of the control group), more AIDS subjects (53%) were impaired than asymptomatic HIV+ subjects, and more asymptomatic HIV+ subjects (29%) were classified as impaired relative to HIV- controls (22%). These differences were statistically significant. McArthur et al. (1989) reported no differences between asymptomatic HIV+ and HIV- controls on

both a screening battery and a more comprehensive battery of neuropsychological measures. The collection of tests used in this study was fairly limited, and was not specifically designed to detect the previously described deficits. As well, subjects were compared on an overall impairment rating whose criterion for inclusion was more stringent than other studies (at least two standard deviations below the HIV-controls' performance on at least two tests). Miller, Satz, and Visscher (1991) reported similar findings, but also had a brief battery and strict criteria for impairment, as did a 1990 study by Selnes and colleagues which also reported no associated cognitive decline. Discrepant findings are often due in part to methodological inconsistencies between studies.

Methodological Considerations

Defining neuropsychological impairment is an area characterized by considerable variability, and often studies reporting no impairment in this patient population use stringent definitions for cognitive impairment. Criteria for a label of "impaired" must be specified and examined before proceeding with a study (Grant and Heaton, 1990). For example, if impairment is classified only at standard deviations of two or more below the normative sample, subtle neuropsychological deficits (as are hypothesized) might elude detection. This criterion, and therefore the results, are clearly dependent upon the author's conceptualization and definition of cognitive impairment. In general, it appears that the majority of studies defining impairment as subtle (generally one standard deviation below the mean of the control group) have demonstrated measurable differences between persons with asymptomatic HIV

infection and HIV- controls. Using one standard deviation is an acceptable way to define impairment (a performance falling below the 16th percentile), as this is the criterion typically used to detect problems in clinical neuropsychological assessment. However, in order for such findings to be clinically meaningful, they would need corroboration by deficient performance on other tests presumed to measure the same cognitive ability. Thus, a person should only be considered "impaired" in a cognitive domain for which they have consistently scored below the 16th percentile on several tasks.

Perhaps a better way to resolve this confound is to respecify what is meant by a performance falling one standard deviation or more below the mean. Considering that the majority of control groups are well-educated and thus often perform above expected levels, comparing performances to these groups effectively makes the label of impairment quite severe. Rather than referring to a score below one standard deviation as an impaired performance, it would be more accurate to simply describe it as a subtle difference. In this way, there is no stigma attached as there might be to words such as "impairment" or "deficit". Few, if any, studies have convincingly shown that these so-called deficits translate into "impaired" daily functioning. Thus, examining "differences" and variables related to them might be less misleading and more productive. The fact that few studies obtain multiple measures of the same ability would likewise support the use of the term "difference", since true impairment can not be determined.

Other methodological concerns include the neuropsychological measures used,

the nature of the control group, sample size, homogeneity of the sample, and exclusion criteria. The neuropsychological tests selected to measure cognitive performance may produce disparate results depending on the cognitive functions the tests are designed to assess, as well as the severity level of the specific cognitive impairment they are capable of detecting (Bornstein, 1994). An extensive battery of tests designed to sample performance on multiple measures of the hypothesized deficits would be more likely to reveal differences between HIV- and asymptomatic HIV+ subjects than would a brief battery which does not include multiple measures of the proposed deficits. In general, most researchers believe the deficits associated with HIV to be subcortical in nature (Navia & Price, 1986; Johnson et al., 1995; Brenn, Eaton, Carlson, & Lott, 1995; Reinvang, Froland & Skripeland, 1991). Thus, measures of attention and concentration, as well as reaction times and psychomotor speed might be important in a comprehensive battery of tests capable of detecting differences.

Different criteria for the selection of comparison groups may also result in disparate findings. Based on the control group's composition, the HIV groups under scrutiny may or may not appear to deviate from the norm (i.e., in most cases, the control group). HIV- controls matched for age and education have been used for comparison, as have the normative samples that were used in the original neuropsychological test construction. If HIV- matched controls are used, the issue of whether the controls are taken from a population similar to the HIV+ population must be considered. Goethe et al. (1989) found no cognitive impairment in their

HIV+ asymptomatic subjects relative to their control group. However, the control subjects had all experienced a head injury involving an average loss of consciousness of 1.57 hours with a range from zero to seven hours. Clearly, findings from a study such as this must be stated with reservation. Karlsen, Reinvang, and Froland (1992) reported on reaction times in asymptomatic HIV+ subjects, and found no difference between their performance and HIV- controls. This study did not, however, consider age or education of subjects, both of which are potentially important when examining neuropsychological performance. However, they did report a clear trend for asymptomatic individuals to have reduced speed and increased variability in reaction time.

The sample size must be large enough to use appropriate statistical procedures from which one can make generalizations. In much of the current research, there are numerous variables (neuropsychological test measures, in particular) which require a large number of subjects in order to have the power to detect differences between groups. A comprehensive battery of neuropsychological tests is necessary to adequately assess cognitive functioning, given that differences between groups are likely to be subtle. This results in a large number of dependent variables. With the exception of a few larger studies (Miller et al., 1990; Ostrow et al., 1989), most have been severely limited by sample size. Homogeneity of the sample is also desired, as factors such as levels of immune system functioning and the presence of opportunistic infections may confuse results when subjects who are at more advanced stages of illness are examined together with asymptomatic HIV+ patients. As well, both ARC

and AIDS are often accompanied by well-documented cognitive impairment and physical symptoms which may confound the results when these groups are combined with asymptomatic HIV+ patients. Strict exclusion criteria are necessary if research is to clarify relationships between cognitive and psychological variables. Including subjects with a history of head injury or psychiatric disorder, for example, would make it difficult to interpret differences between groups, although these groups warrant separate examination as well. Both Van Gorp, Lamb, & Schmitt (1993) and Bornstein (1994) review these methodological issues in considerable detail.

Possible Neurological Causes of Cognitive Dysfunction

Given some indication of subtle, yet demonstrable, cognitive differences, it is important to examine the possible causes for this phenomenon. While the HIV-virus itself, or adventitious diseases associated with the virus, may indeed be responsible for neuropsychological dysfunction, there are alternative explanations which have yet to be thoroughly explored. These include emotional and psychological distress, which may be associated with any chronic and progressive disease. These possible causes will be discussed later. Other factors to consider are the patient's knowledge of his/her HIV status, level of immune system function, and duration of infection.

There has been evidence reported in the literature to suggest that HIV may have detectable neurological correlates, even when patients are classified as "asymptomatic". Abnormal computerized tomography (CT) scans have been seen in HIV+ patients, as have other subclinical neurological abnormalities (Carne et al., 1989). Electroencephalographic (EEG) anomalies have also been demonstrated in

individuals with asymptomatic HIV infection, as have otoneurologic abnormalities (based on deficits noted in audiologic and vestibular examinations) (Koralnik et al., 1990). Such studies suggest that the virus may invade neurological structures at early stages of infection. Resnick, Berger, Shapshak, and Tourtellotte (1988) reported evidence supporting the notion that the HIV virus penetrates the blood-brain-barrier even at asymptomatic stages of infection. This invasion may initially manifest itself functionally rather than structurally, appearing as cognitive impairment. Martin et al. (1993) reported a subgroup of HIV infected subjects who were characterized by poor acquisition of a motor skill, slowed reaction time, and elevated levels of quinolinic acid in their cerebrospinal fluid. They described these deficits as consistent with dysfunction in the basal ganglia. Carne et al. (1989) found abnormal computerized tomography (CT) scans in 20% of their small asymptomatic HIV+ sample, and concluded that the virus is capable of causing nervous system changes even at the time of seroconversion. Another study found no difference in Magnetic Resonance Imaging (MRI) results between groups of HIV-, asymptomatic HIV+, and AIDS subjects (McAllister et al., 1992). However, this study failed to exclude subjects with a history of head injury, epilepsy, psychiatric history, or intravenous drug use. Koralnik et al. (1990) also failed to find MRI differences between asymptomatic HIV+ and HIV- subjects. Cortical atrophy was noted on magnetic resonance studies of asymptomatic HIV+ patients in a study by Handelsman et al. (1993), although these patients also had a history of drug abuse.

While there is certainly evidence that HIV can invade the central nervous system

(CNS) and cause changes early in the course of infection (Price et al., 1988), it does not appear that these neurological markers are necessarily related to cognitive functioning in a systematic way. According to several studies, cognitive performance does not appear to be related to level of immune function as measured by CD4 and CD8 lymphocyte counts. That is, within asymptomatic patients, markers of immune function such as CD4 and CD8 lymphocyte counts do not appear to be correlated with either neuropsychological performance (Bornstein et al., 1991; Gibbs et al., 1990; Martin et al., 1993; McArthur et al., 1989; Miller et al., 1990; Podraza et al., 1994) or reaction times (Karlsen et al., 1992; Karlsen et al., 1993). Perry and his colleagues (1989) suggested that to use these immune measures to screen for cognitive functioning in asymptomatic HIV infection would be inappropriate, given the lack of evidence for a correlation between these two variables.

Likewise, cerebral spinal fluid (CSF) abnormalities were not related to neuropsychological performance in asymptomatic HIV+ subjects in studies conducted by Goethe et al. (1989) or McArthur et al. (1989), nor were neurological symptoms related to cognitive functioning on a brief battery of neuropsychological tests in a group of asymptomatic HIV+ and generalized lymphadenopathy subjects (Janssen et al., 1989). Cognitive functioning is not related to time since seroconversion (i.e. the duration of infection is not related to increasingly poorer performance on cognitive measures) nor to knowledge of serostatus within the group labelled asymptomatic (i.e a subject's awareness of whether or not he/she is HIV+ is not related to cognitive performance) (Janssen et al., 1989). Miller et al. (1990)

likewise found duration of illness to be unrelated to cognitive functioning. One study did report findings contradictory to these conclusions in a sample of asymptomatic men (Bornstein, Nasrallah, Para, Whitacre, & Fass, 1994), but overall the consensus would appear to be that differences in cognitive functioning are not a simple function of the length of illness.

Alcohol and drug use (although in most studies subjects who are classified as abusers are excluded) are also possible confounds, as their use and abuse has been shown to affect cognitive functioning in non-HIV infected individuals (Berry et al., 1993; O'Malley, Adamse, Heaton, & Gawin, 1992; Ardila, Roselli, & Strumwasser, 1991; Lewis & Hordan, 1986). However, Bornstein, Fama, et al. (1993) found that neither recency nor severity of substance abuse accounted for the differences in neuropsychological performance between asymptomatic HIV+ subjects and HIV- subjects. Grant et al. (1987) and McArthur et al. (1989) reported similar results.

Antiretroviral therapy (e.g. azidothimidine [AZT], and other drugs which are believed to inhibit the reverse transcriptase enzyme required by HIV for replication, in the hopes of retarding disease progression) also does not seem to mediate cognitive differences (Skoraszewski, Ball, and Mikulka, 1991; Gorman et al., 1993; Egan, Brettle, & Goodwin, 1992) or differences in reaction times (Karlsen et al., 1993; Perdices & Cooper, 1989), although little research has specifically examined these issues in asymptomatic populations. Reidel et al. (1992) reported improvements in neuropsychological symptoms for 458 of 468 HIV seropositive patients who were receiving azidothimidine (AZT) treatment. Thus, it might be

suggested that should AZT have a positive effect on neuropsychological performance, differences between asymptomatic HIV+ and HIV- subjects on cognitive tasks might in fact be minimized by AZT therapy and make detection of the proposed deficits more elusive. Schmitt et al. (1988) also found improved cognition with antiretroviral therapy in AIDS patients. This study attributed some of the improvement to concurrent decreases in symptomatic distress, thus lending evidence to a link between distress and cognitive performance in HIV infection.

Possible Psychological Causes of Cognitive Dysfunction

With regard to psychological factors which may affect cognitive performance, it appears that depression is more evident in the asymptomatic stage of HIV infection, and, generally, is more common in the homosexual population as compared to the heterosexual population. In a well-controlled study by Perkins et al. (1994), they showed both asymptomatic HIV+ and HIV- homosexual men to have higher lifetime prevalence rates for major depression in comparison to the general population. Williams, Rabkin, Remien, Gorman, and Ehrhardt (1991) reported similar rates. Thus, the sample of males typically studied to date (i.e., homosexual), are at greater risk of depression than their heterosexual counterparts regardless of HIV status. The findings of Ostrow et al. (1989) corroborate this assertion. Lunn et al. (1991) reported higher rates of depression and anxiety in asymptomatic HIV+ subjects than in AIDS or HIV- subjects. Marsh and McCall (1994) reported higher rates of depression as measured by the Beck Depression Inventory (BDI) in asymptomatic HIV+ subjects when compared to HIV- controls, although this sample was extremely

small. Martin et al. (1993) reported similar findings, although their cohort was comprised of subjects at all stages of HIV infection (asymptomatic, ARC, and AIDS).

Depression and Neuropsychological Performance

Despite increased depression, numerous studies have shown that depression does not appear to be directly related to the demonstrated cognitive impairment associated with HIV infection. Bornstein, Pace, et al. (1993) reported that regardless of whether organic symptoms of depression were excluded or included, there was no relationship between severity of depression and neuropsychological performance. Gibbs et al. (1990) likewise found no relationship between depression as reported on the Beck Depression Inventory (BDI) and neuropsychological measures when examining HIV-, HIV+, and ARC subject groups. In a study using the Profile of Mood States (POMS) depression-dejection subscale as a measure of depression, this measure and tests of cognitive functioning each explained unique variance in the subjects' performance, once again leading to the conclusion that depressed mood and cognitive impairment are not systematically related (Grant et al., 1993). Hinkin et al. (1992) found no differences between depressed HIV+ subjects and nondepressed HIV+ subjects on a reasonably extensive neuropsychological test battery, nor did Karlsen et al. (1992) find a correlation between depression as measured by the POMS and reaction times in asymptomatic HIV+ subjects. Kovner et al. (1989) found that a mixed group of HIV infected subjects evidenced cognitive impairment which was not related to mood or increased anxiety as measured by the depression

and psychasthenia scales of the Minnesota Multiphasic Personality Inventory (MMPI). Likewise, Atkinson et al. (1988) found no difference in levels of neuropsychological impairment between HIV+ subjects with and without a lifetime history of major depression, substance-use disorder, or generalized anxiety disorder. This particular study looked at all stages of HIV infection simultaneously. Lunn et al. (1991) found that covarying out measures of depression and anxiety did not impact on the significance nor the tendency for HIV+ subjects to do more poorly on measures of psychomotor speed and verbal memory than HIV- controls. When Mapou et al. (1993) examined relationships between depression (as measured by the Beck Depression Inventory [BDI]) and anxiety (as measured by the State-Trait Anxiety Inventory - STAI-T) and neuropsychological performance, no significant correlations were found. Their subject group was heterogeneous, in that they comprised all stages of HIV infection. However, this study did not employ strict exclusion criteria, such as head injury or substance abuse, and had a relatively small sample size.

Thus, there appears to be an overwhelming consensus that depression is not systematically related to decrements in cognitive performance on neuropsychological measures in HIV+ subjects. These findings are surprising, given past reports which suggest that depression typically has an adverse effect on at least selected areas of neuropsychological performance in non-HIV infected subjects (Fisher, Sweet, & Pfaelzer-Smith, 1986; Newman & Sweet, 1986). However, some researchers have postulated that depression may only reliably produce this effect in an elderly

population (Cassens, Wolfe, & Zola, 1990). Persons infected with the HIV virus are most often young and have not experienced previous diseases that have compromised their cognitive functioning. As suggested by Hinkin et al. (1992), this discrepancy between findings that depression may or may not impact on cognitive functioning may be due to a meaningful difference on cognitive measures between persons with an adjustment disorder with depressed mood and those with a major depressive disorder. Persons with HIV infection are most likely suffering from an adjustment disorder with features of depression, rather than a mood disorder. The lack of correlation between depression and neuropsychological performance in HIV+ subjects would appear to be robust.

Some studies, however, do not report differences in overall depression between HIV- and HIV+ subjects (Janssen et al., 1989; Beason-Hazen, Nasrallah, & Bornstein, 1994). Beason-Hazen et al. (1994) also found depression to increase and neuropsychological performance to decrease as the patient's self-reported current symptoms increased. However, depression was not responsible for the relationship between cognitive variables and self-reported symptoms. There is some evidence which suggests that higher levels of depression are indeed related to higher levels of cognitive complaints in HIV+ subjects, but this finding does not necessarily generalize to objective neuropsychological data (van Gorp et al., 1991).

General Psychological Distress in HIV Infection

Although depression alone does not appear to account for cognitive impairment, more general psychological distress may. Global psychological distress is more

prevalent in the HIV+ homosexual population when compared to HIV- homosexual controls (Fitzgibbon et al., 1989). This might be attributed to the presence of a life-threatening disease and thus would be expected in other serious illnesses. However, in a study by Kelly et al. (1991), men with asymptomatic HIV infection were significantly more distressed than was a group of male cancer patients. It would seem the level of distress associated with HIV infection is even higher than that reported in conjunction with other illnesses, perhaps because of the stigma surrounding a diagnosis. It would appear that not only homosexual men, but men and women who are at risk for HIV infection for any number of reasons (e.g., intravenous drug use, sexual contact with an HIV+ individual) also have a higher incidence of DSM-III-R Axis I diagnoses (Perry et al., 1990). This study rated subjects before they were informed of their serostatus, and also reported higher rates of Axis I diagnoses prior to antibody testing in homosexual/bisexual men who eventually tested positive as compared to a similar sample who were not infected. Similar findings, with regard to increased rates of psychopathology in high-risk individuals were reported by Rosenberger et al. (1993). Both Atkinson et al. (1988) and Skoraszewski et al. (1991) indicated greater measures of overall psychological distress as reported on the Symptom Checklist-90-Revised (SCL-90-R) in all groups of HIV infected subjects when compared to HIV- controls.

There is also increasing evidence that people with asymptomatic HIV infection experience psychopathology and distress equal to or greater than that found in persons with ARC or AIDS. This may be due to the "Sword of Damocles" syndrome

(Perry & Tross, 1984) which suggests that these people experience greater anxiety because of the uncertainty surrounding the inevitable onset of symptoms. Thus, within the homosexual population, which has more frequent psychiatric impairment, those infected with the HIV virus and at the asymptomatic stage seem to be at even greater risk for psychological distress. Wilkins et al. (1991) found that even within a group of 39 HIV+ subjects who did not report cognitive complaints, 59% met criteria for the presence of a psychiatric disturbance (primarily, major depression) within the previous six months. Subjects reporting cognitive difficulties had even higher rates of psychopathology, with 82% meeting the DSM-III criteria for at least one of several designated psychiatric diagnoses in the preceding six months (major depression, post-traumatic stress disorder, bipolar disorder, schizophrenia, alcohol/drug abuse/dependency, generalized anxiety disorder, or panic disorder). Lunn et al. (1991) reported asymptomatic HIV+ subjects as having higher levels of anxiety and depression as reported on the SCL-90-R than either HIV- controls or AIDS subjects.

Conversely, data reported by Rosenberger et al. (1993) and Williams et al. (1991) suggest that although prevalence of psychiatric disorder is higher in homosexual males when compared to the general population, there appears to be no difference in rates between HIV+ and HIV- homosexual males, or between HIV+ homosexuals at different stages of infection. These studies assessed psychiatric disorders as diagnosed by a clinician. It would be informative to examine these issues by assessing self-report of general psychological distress, rather than strictly defined

major psychopathology. There is considerable room for psychic pain between a psychologically well person and one who meets criteria for a legitimate psychiatric disorder.

Cognitive Dysfunction and its Relation to Perception of Daily Functioning

An increase in cognitive dysfunction does seem to be related to an elevation in patients' negative perceptions of their daily functioning. In previously reported data from an asymptomatic HIV+ subject group, Bornstein, Nasrallah, et al. (1993) found that impairment was related to self-reported daily functioning as measured by the sickness impact profile (SIP). As neuropsychological impairment increased, reported problems with daily functioning did as well, even after controlling for age, education, depression, and weekly alcohol consumption. Thus, although differences have not always been described as clinically relevant, some subjects seem to perceive them as such. Another study utilizing this same data base (Beason-Hazen et al. 1994) found a correlation between neuropsychological performance and currently reported subjective complaints of neurological symptoms, even after controlling for depression. The strongest relationships in this study were between general physical symptoms and information/processing speed and reaction time measures.

An additional study using a different data base found that self-reported cognitive complaints increased steadily between HIV-, HIV+, and ARC patients (Gibbs et al., 1990). In Mapou et al.'s study (1993) of HIV infection, a relationship was reported between subjects' self-reported cognitive and motor complaints and depression and

anxiety. As well, HIV+ subjects complained of more difficulty than HIV- controls in areas of sleep and arousal, motor and sensory functioning, somatic complaints, spatial awareness, language, memory, and mood. When HIV+ subjects were divided into two groups based on the presence or absence of complaints, the group with complaints had poorer performance on neuropsychological measures of response speed, motor function, and memory, suggesting an accurate self-assessment. These relationships were shown to be independent of the relationship between mood and cognitive functioning.

These studies lend credence to the notion that though cognitive deficits may be subtle, they do seem to have some impact, or are at least related in some way, to daily functioning. The question remains as to whether or not general psychological distress plays a role in these observed relationships. Some studies have failed to find this relationship. A heterogeneous group of asymptomatic, ARC, and AIDS subjects, divided into two groups based on the presence or absence of cognitive impairment, was found to show no significant relationship between their number of cognitive complaints and neuropsychological impairment (Wilkins, 1991). An examination of these relationships within a homogeneous sample would help to clarify the issue.

Relationship Between General Psychological Distress and Cognitive Functioning

The issue the present study seeks to examine is whether a subject's perceived severity of global psychological distress, as measured by the SCL-90-R, accounts for a major portion of neuropsychological performance in areas of cognitive functioning including memory, executive functioning, attention and concentration, psychomotor

speed, and reaction time. Wolf et al. (1991) described significant relationships between psychological distress, as measured by the Symptom Checklist 90 (SCL-90) and several cognitive measures, including free recall total from the Buschke Selective Reminding Test, dominant hand finger tapping, and WAIS-R digit symbol. This study, however, examined a heterogeneous subject group that included both asymptomatic and symptomatic HIV infected individuals, and had a limited number of subjects (n=29). It would be interesting to examine these relationships in a larger, more homogeneous subject group.

Skoraszewski et al. (1991) found that psychological distress did not (after covarying out SCL-90-R measures) influence impairment ratings which differentiated groups of HIV-, HIV non-AIDS, and AIDS subjects. This study was limited by a small sample size and an abbreviated neuropsychological test battery. Atkinson et al. (1988), using a heterogeneous group of HIV infected individuals, reported no difference in psychiatric disorder between subjects who were and were not cognitively impaired. Again, asymptomatic subjects were not examined alone, and the number of subjects was quite restricted. This study also neglected to exclude subjects who had a history of head injury. Hence, the relationship between general psychological distress and cognitive functioning certainly requires greater clarification.

It is therefore of interest to look at the actual relationships, as well as the extent and direction of any observed relationships, between objective neuropsychological measures and subjective global psychological distress within one homogeneous group - asymptomatic HIV+ subjects. Heterogeneous groups have inherent confounds, and

generalizations to specific subgroups within HIV infected individuals are all but impossible to achieve. Thus, asymptomatic HIV infection merits selective examination. Using groups of asymptomatic HIV+ and HIV- homosexual and bisexual men, this study examined relationships between measures of subjective global psychological distress (SCL-90-R) and performance on a selected battery of objective neuropsychological tests designed to detect subtle neurocognitive differences between groups. It is hypothesized that observed group differences on measures of cognitive functioning (specifically attention/concentration) are mediated in part by subjective psychological distress. In other words, asymptomatic HIV+ subjects may display poorer performance on cognitive tests because they are experiencing greater distress. This information would be of value for several reasons. First, subtle cognitive dysfunction early in the course of infection may be predictive of future cognitive decline. An ability to predict would be useful in that support services might be provided at the asymptomatic stage of infection in an effort to delay disease progression, or at least to help the affected person plan for his or her future. Second, it is worthwhile to examine subtle cognitive differences in greater detail in an effort to clarify relationships between HIV infection and cognitive functioning. Since this is an area of considerable debate, information which can not only shed light on this subject, but also suggest implications for future research as well as clinical practice, is greatly needed.

Method

Subjects

The sample consisted of 140 asymptomatic HIV+ homosexual and bisexual men with a mean age of 33.12 years. The control group was composed of 82 HIV- homosexual and bisexual men with a mean age of 31.90 years. Demographic variables are presented in Table 1. There was a statistically significant difference between groups on education. The HIV- subjects, with a mean of 14.57 years of education (SD=2.27), were significantly more educated ($p<.014$) than the HIV+ subjects, who had a mean education of 13.75 years (SD=2.44). Full scale IQ (as measured by the Wechsler Adult Intelligence Scale-Revised) did not differ significantly between groups. T4 lymphocyte counts (a measure of immunosuppression) were significantly different between groups. This difference is expected, as the HIV virus acts to decrease immune functioning in those infected with the virus.

Table 1
Means, standard deviations, and significance values for demographics of asymptomatic HIV+ and HIV- subjects.

	HIV+ (n=140)	**HIV- (n=82)**	***p* value**
Age	33.12 (6.98)	31.90 (9.00)	N.S.
Education	13.75 (2.44)	14.57 (2.27)	.014
FSIQ	103.39 (13.99)	106.44 (12.66)	N.S.
T4 Count	523.68 (227.36)	943.00 (142.35)	

Subjects were part of a longitudinal study of the neuropsychological, psychosocial, and neuropsychiatric effects of HIV infection conducted at the Ohio State University (Columbus, Ohio). Subjects were recruited from several sources, including an AIDS clinical trials unit (ACTU), advertisements in publications within the gay community, word of mouth, and contact with local HIV community-based support groups. No subjects were included who reported a history of intravenous drug use, head injury involving loss of consciousness greater than one hour, or any neurological disease. Asymptomatic subjects did include those with generalized lymphadenopathy, but no other symptoms related to HIV infection were present. There was no attempt to select or exclude subjects who showed signs of either neurobehavioural or psychological impairment.

Measures

Neuropsychological Measures. The neuropsychological measures used were selected on the basis of their demonstrated sensitivity in detecting the subtle neurocognitive deficits believed to characterize cognitive performance in some asymptomatic HIV+ patients. These included the following:

Test of general cognitive ability.

1. Wechsler Adult Intelligence Scale - Revised (WAIS-R; Wechsler, 1981). This test, comprised of 11 subtests, was used to determine a subject's overall IQ. It covers numerous cognitive abilities including verbal comprehension, visuo-spatial skills, processing speed, and freedom from distractibility.

Tests of executive functioning and concept formation.

1. Wisconsin Card Sorting Test (WCST; Robinson et al., 1980). This test requires a subject to sort cards by color, number, or shape, depending upon the principle in effect at any given time. The subject must determine the criteria for sorting based only on responses of "correct" or "incorrect" from the examiner. Skills such as mental flexibility and problem solving are measured by this task.

2. Verbal Concept Attainment Test (VCAT; Bornstein & Leason, 1985). This test measures a subject's ability to make generalizations and to abstract by requiring subjects to group words within a list according to some commonality.

3. Verbal Fluency (VFT; Borowski, Benton, & Spreen, 1967; Benton, 1968). Spontaneous production of words is recorded by asking subjects to name as many words as they can beginning with a specified letter within a given time frame. This task measures mental flexibility, verbal fluency, and organization of verbal recall.

4. Figural Fluency Test (FFT; Ruff, Light, & Evans, 1987). The visual correlate of the verbal fluency task, this test requires subjects to form as many unique designs as possible, given only random patterns of dots, within a certain amount of time.

Tests of verbal memory.

1. Selective Reminding Test (SRT; Buschke & Fuld, 1974). This verbal memory task requires subjects to memorize a list of 12 unrelated words. After each trial, the words they failed to repeat are said once more, and they attempt to recall the entire list. 12 trials are given, followed 30 minutes later by a free recall task, a

cued recall task, a multiple choice recall task, and a recognition task.

Tests of speed of processing and attention/concentration.

1. Paced Auditory Serial Addition Test (PASAT; Gronwall & Wrightson, 1981). This measure of attention requires subjects to add numbers presented serially. There are four trials, with faster presentation of numbers in successive trials. This task measures speed of processing and attention and concentration.

2. Trailmaking Test, parts A & B (Trails A, Trails B; Lezak, 1983; Reitan & Wolfson, 1985). In Part A, subjects must connect circles with numbers in them in serial order as quickly as they can. Part B requires the subject to alternate between successive numbers and letters. To perform well, a subject must think quickly and attend to the task.

3. Visual Memory Span, forward and backward, from Wechsler Memory Scale - Revised (WMS-R - VSF, VSB; Wechsler, 1987). This task requires a subject to watch the examiner touch a series of squares in a specific order, and then to immediately repeat this sequence. Immediate visual memory and attention is measured.

Tests of motor coordination and reaction time.

1. Grooved Pegboard (Pegs; Lezak, 1983; Heaton, Grant, & Matthews, 1986). This test of motor coordination requires subjects to place key-shaped pegs in a board as quickly as they can.

2. Simple, choice, and go-no-go reaction time measures. Reaction time measures required the participant to depress a key immediately upon seeing a

designated bulb light. These measures have been found to measure a unique cognitive function that is not necessarily represented in a standard neuropsychological battery (Miller et al., 1991). Thus, it is important to include these measures in order to comprehend more fully the nature of potential cognitive deficits.

The total time to complete the battery was approximately four hours.

Psychological Distress. Psychological distress was measured by the Symptom Checklist 90 - Revised (SCL-90-R; Derogatis, 1977). This measure is comprised of 90 items which are scored by the respondent on a 5-point Likert scale according to the degree to which the symptom is present. These items are then divided into the following nine dimensions: somatization, obsessive-compulsiveness, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. A global measure of the intensity of psychological distress can also be derived (Global Severity Index - GSI). The SCL-90-R has been shown to be both a valid and reliable measure. Internal consistency coefficients have been shown to range from .77 to .90 for the nine subscales (Derogatis, Rickels, & Rock, 1976; Horowitz, Rosenberg, Baer, Ureno, & Villasenor, 1988). Test-retest coefficients were determined by Horowitz et al. (1988) using an interval of ten weeks, and were found to be acceptable, ranging from .70 to .83 on the subscales, and .84 for the GSI. Peveler and Fairburn (1990) conducted research to examine the scale's concurrent, predictive, and construct validity. The SCL-90-R appeared to correspond with the results of the Present State Examination. Predictive and construct validity were also established using diabetic and bulimic samples. The MMPI was used by Derogatis

et al. (1976) to confirm convergent-discriminant validity. Each SCL-90-R scale was most highly correlated with its corresponding MMPI clinical scale. This instrument, specifically the total mean score (i.e., GSI), was used to detect both symptomatic psychological and emotional distress.

Procedure

Subjects were assessed at the Ohio State University (Columbus, Ohio) over the period of a day. All participants were given literature describing the nature of the study and all gave written informed consent. Participation was fully voluntary, and did not affect a subject's eligibility to receive treatment at the University. To determine each participant's serostatus, enzyme-linked immunosorbant assay (ELISA) was used, and positive results were confirmed by Western Blot. These are standard laboratory procedures used to confirm a diagnosis of HIV infection using patient blood samples. All neuropsychological tests were administered using standardized forms and procedures by trained research assistants. Each subject received a stipend of $100. Scoring of tests was performed by a research assistant, and then checked for accuracy by another trained assistant. The author assisted in the collection of the data presented here, but was not involved in the original design of the project or selection of measures.

Results

Psychological Distress Variable. The means for both groups on the SCL-90-R are presented in Table 2. On cursory inspection, it is evident that men with HIV infection are reporting increased levels of psychological distress. However, this finding is only a trend, as it does not reach statistical significance.

Table 2

Mean and standard deviation for psychological distress measure (SCL-90-R) by group (asymptomatic HIV+ and HIV-).

	HIV+ (n=140)	**HIV- (n=82)**
SCL-90-R Total Mean Score	.73 (.60)	.58 (.51)

Cognitive Impairment Variables. Several decisions were made concerning variable groupings prior to statistical analysis. First, a Principal Components Analysis with varimax rotation was performed on the neuropsychological test variables, using the raw test scores for the entire sample. The Statistical Package for the Social Sciences, version 5.1, was used for statistical analysis. The means and standard deviations of the raw scores for each neuropsychological test measure used in the factor analysis are presented by group in Table 3. Upon cursory inspection of these means, one can see that there is a very subtle, yet consistent trend towards decreased performance in the asymptomatic group. The results of the Principal Components Analysis (PCA) with varimax rotation indicated that this battery of tests represented 5 cognitive domains accounting for 67.1% of the variance. Exploratory analyses using

a maximum likelihood factor analysis approach, which allows for error within each test measure, produced a factor structure virtually identical to the solution found using PCA. These domains, the test measures comprising them, and their respective factor loadings are displayed in Table 4. Factor scores were used in all subsequent analyses involving cognitive variables.

Rationale for Statistical Analysis

Because the two groups differed significantly in years of education, it was necessary to control statistically for this variable. This seemed an appropriate precaution, as many neuropsychological measures are correlated with attained educational level (Heaton et al., 1986). Should education prove to be related to the neuropsychological measures used in this study, it is imperative that this potential confound be accounted for prior to examining group differences in cognitive functioning. In order to determine the amount of variance in each neuropsychological domain accounted for by years of education, a series of hierarchical multiple regression were used in which each cognitive domain was predicted utilizing years of education as the first predictor.

Following this statistical control for education, relationships between psychological distress and the five cognitive domains were examined using the same multiple regression procedure and adding the additional independent variables. The total mean score for the SCL-90-R was entered on the second step. Lastly, to observe whether or not any remaining variance in cognitive functioning could be accounted for by HIV status, the variable designating group was entered into the multiple

regression equation on the third step. A multiple regression equation was determined for each of the five cognitive domains as they were statistically independent factors. In sum, this statistical procedure controlled for education by removing the variance accounted for by this measure from the cognitive domains, then determined the amount of variance remaining in cognition accounted for by psychological distress, and finally calculated the remaining variance accounted for by group. Thus, to conform to the original hypothesis, any given cognitive domain should have a significant portion of its variance accounted for by the SCL-90-R variable, with no additional variance accounted for by group.

Effects of Education

As predicted, education was significantly related to four of the five cognitive domains: reaction time (R^2 =.0170; $p<.0546$), attention/speed of processing (R^2 =.1021; $p<.0000$), verbal memory (R^2 =.0543; $p<.0005$), and executive function (R^2 =.0330; $p<.0072$). Each of these relationships was in the expected direction, that is, fewer years of education were associated with worse performance on neuropsychological tasks in the cognitive domain.

Effects of Psychological Distress

Psychological distress contributed to a significant portion of the variance in tasks of executive function (R^2 =.0511; $p<.0444$). The finding for attention/speed of processing tasks approached significance (R^2 = .1162; $p<.0657$). For these domains, an increase in subjective levels of distress was associated with decreased cognitive performance.

Table 3

Means and standard deviations for raw neuropsychological test scores by group (asymptomatic HIV+ and HIV- subjects).

Neuropsychological Variables	HIV+ (n=140)	HIV- (n=82)
WCST (cards)**	100.27 (22.59)	102.67(23.14)
WCST (perseverations)**	6.69 (7.98)	7.35 (9.22)
VCAT	20.00 (2.60)	20.41 (2.66)
Verbal Fluency	66.36 (27.16)	71.74 (24.23)
FFT	7.81 (7.80)	8.01 (8.33)
Visual Span (forward)	6.02 (1.06)	6.18 (1.28)
Visual Span (backward)	5.76 (.90)	5.87 (1.02)
SRT (recall)	112.31 (15.60)	118.00(13.08)
SRT (delay)	9.82 (2.20)	10.44 (1.95)
Trails A**	23.73 (6.62)	21.85 (6.63)
Trails B**	58.81 (20.54)	51.63 (16.98)
PASAT (2.4 sec)	38.04 (12.35)	40.34 (11.77)
PASAT (2.0 sec)	34.80 (8.69)	36.96 (9.51)
PASAT (1.6 sec)	28.61 (8.00)	30.91 (8.32)
PASAT (1.2 sec)	20.86 (7.38)	22.70 (6.86)
Simple Reaction Time (dom. hand)**	.47 (.08)	.45 (.08)
Simple Reaction Time (nondom. hand)**	.47 (.08)	.46 (.09)
Choice Reaction Time**	.59 (.08)	.57 (.08)
Pegs (dom. hand)**	65.86 (9.75)	62.24 (8.02)
Pegs (nondom. hand)**	71.69 (12.24)	68.60 (10.23)
RFFT (unique designs)	91.21 (23.02)	102.57(19.86)
Go-No-Go Reaction Time**	.58 (.11)	.59 (.11)
SRT (cued recall)	9.71 (1.67)	10.09 (1.37)

** = **lower** scores are indicative of **better** performance

Table 4

Results of Principal Components Analysis on neuropsychological variables.

COGNITIVE DOMAINS	FACTOR LOADINGS
Reaction Time	
simple reaction time - dom. hand	.90179
simple reaction time - nondom. hand	.91716
choice reaction time	.85941
go-no-go reaction time	.87640
Attention/Speed of Processing	
PASAT - 2.4 sec	.61782
PASAT - 2.0 sec	.83989
PASAT - 1.6 sec	.87020
PASAT - 1.2 sec	.80372
trail making test - part A	-.52931
Verbal Memory	
SRT - total words recalled	.86374
SRT - cued recall	.82455
SRT - delayed recall	.86570
Motor Speed/Attention	
trail making test - part B	.56709
grooved pegboard - dom. hand	.74772
grooved pegboard - nondom. hand	.78177
Executive Function	
WCST - cards	.87810
WCST - perseverations	.88895

Effects of Group

HIV status, as indicated by group, predicted a significant measure of the variance on motor speed/attention tasks (R^2 =.0382; $p<.0111$). The HIV+ patients performed more poorly on these tasks than the HIV- control group.

Summary of Findings by Cognitive Domain

Differences in reaction time and verbal memory between groups were accounted for solely by educational level. For these areas, neither psychological distress nor HIV status appeared to account for a significant portion of the variance between groups.

For measures of executive function, findings suggested that while some variance was again accounted for by years of education, the degree of self-reported psychological distress also contributed to differences between groups. Similar findings were noted for tasks requiring attention/speed of processing. However, variance accounted for by distress only approached significance in this domain. Table 5 indicates the percent of additional variance accounted for by each dependent variable using a model in which education is entered first, psychological distress second, and HIV status last.

HIV status was responsible for variation between groups on measures of motor speed/attention, even after the effects of education and psychological distress were taken into account.

Table 5

Percent of variance in each cognitive domain accounted for by years of education, additional amount accounted for by adding psychological distress, and finally HIV status.

	Education	SCL-90-R	HIV Status
Reaction Time	2%*	1%	0%
Attention/Speed of Processing	10%*	1%**	0%
Verbal Memory	5%*	0%	0%
Motor Speed/Attention	1%	0%	3%*
Executive Function	3%*	2%*	1%

* $p < .05$
** $p = .0657$

Discussion

One of the most robust findings in the study is the relationship between years of education attained and neuropsychological performance, even though the groups did not statistically differ on a measure of intelligence. Education accounted for a significant proportion of the variance in performance on measures of reaction time, attention/speed of processing, verbal memory, and executive function, such that a higher educational level was associated with better objective neuropsychological performance. There appeared to be some indication of a deleterious effect of increased psychological distress on cognitive performance. This was noted on measures of executive function and to a lesser extent on tasks requiring attention/speeded processing. Overall, there was little difference between groups on a measure of general subjective psychological distress. However, psychological distress, though not statistically significant between groups, did appear to play some mediating role in the aforementioned cognitive domains.

Once education and psychological distress were accounted for, HIV status contributed to a significant proportion of the variance on motor speed/attention measures. In fact, in this domain, group membership appeared to be the only variable examined that contributed to this observed difference. Neither education nor psychological distress seemed to mediate performance on these tasks (neither was found to contribute a significant amount of variance). Conversely, and in concurrence with the original hypothesis, group effects were not evident on executive function measures or on measures of attention and speeded processing once

psychological distress was taken into account.

Findings of decreased performance on executive function and attentional measures in men with asymptomatic HIV infection, though statistically meaningful, should not be taken as evidence for impaired daily functioning. Instead, these decrements might manifest themselves only when a cognitive demand is made more difficult by the addition of a task to be performed simultaneously, or when there is time pressure. For example, these differences might manifest themselves, if at all, only when the person finds it necessary to do two tasks at once, attend to very complex information, or solve problems that require close attention to detail. It is important to examine the possibility that the memory problems reported in previous studies may in fact result from compromised attention and executive functioning, rather than from a specific cortical deficit. That is, information which is not properly attended to and encoded at the time of presentation may be more difficult for the patient to retrieve. For example, in order to remember an appointment, a person must first attend to the speaker so they can encode the date and time.

The results of the analyses are somewhat difficult to interpret, since there are no consistent patterns across cognitive domains. It is interesting, though, that despite the failure to detect significant differences between groups on all cognitive domains, an examination of the means of raw test scores reveals a subtle yet consistent trend toward decreased performance in the HIV+ group. However, when compared to normative data, these decrements are not at a level which would be indicative of clinical impairment. It is possible that this trend is accounted for by education and

IQ differences. That is, the group with consistently lower neuropsychological test scores also had fewer years of education and a lower overall IQ. Nonetheless, several conclusions can be drawn from the results of statistical analysis, each with implications for both HIV infection and future research.

First, neuropsychological performance seems highly dependent upon educational level. The findings of Heaton et al. (1986) are consistent with these findings. These authors emphasize that education is not only related to simple motor and sensory tests, but is particularly associated with verbal skills and knowledge which was gained in the past. This would certainly account for past findings which suggest deficits in verbal memory. It is interesting that past research on cognitive differences has often failed to control for education, even going so far as to declare that seemingly small yet significant differences in level of education are not clinically meaningful and may thus be legitimately ignored in analyses. Perhaps previous studies finding neuropsychological impairment in asymptomatic HIV+ patients were in fact detecting subtle differences in educational level.

This study was composed of subjects who were generally well-educated. It is possible that cognitive deficits associated with HIV infection might be more pronounced in a sample of less educated subjects, as it has been hypothesized that these individuals have less "cognitive reserve" and are thus at increased risk for neurobehavioral complications. Silva et al. (1995) reported that in their sample of asymptomatic HIV+ men, neuropsychological impairment was most evident in those with less cognitive reserve. Reserve was defined by education, occupational

attainment, and premorbid IQ. These researchers suggested that covarying for these effects might not be recommended, because education along with the other variables seem to affect different groups of HIV+ patients differently. It is interesting that in this study, retesting of subjects did not indicate that those with less cognitive reserve declined at a faster rate. The conclusions of this study regarding the importance of cognitive reserve are similar to those of Satz et al. (1993), who reported that years of education and, more generally, cognitive reserve, are important variables when examining cognitive performance. It would be prudent for future studies to carefully consider not just education, but other variables contributing to cognitive reserve.

The finding of decreased performance by the HIV+ group on measures of motor speed/attention appeared to be robust, and not subject to mediation by education or psychological distress. It is important to note that while these results are statistically significant, these problems do not necessarily preclude daily functioning. However, problems might only be noted when a task demanding a high level of eye-hand coordination (e.g., sewing a button on a shirt) must be performed quickly. One explanation for decreased motor speed is that the HIV virus is in someway interfering with motor functioning, which is conceivable since the HIV virus has been detected shortly after seroconversion in the cerebrospinal fluid of infected patients (Resnick et al., 1988). The tasks that comprised this domain all involved eye-hand coordination in addition to motor speed. When examining P300 latencies (expected changes in the brain's electrical activity when repeatedly exposed to target and non-target stimuli) in individuals with asymptomatic HIV infection, Ollo, Johnson, and

Grafman (1991) found that these subjects had significantly smaller amplitudes and delayed latencies for visual stimuli than their HIV- group. These findings were present in the absence of any detectable neuropsychological impairment, suggesting that basic cognitive or perceptual processes (such as those involved in the evaluation of visual stimuli) might be affected by the virus before the onset of objective cognitive dysfunction. Perhaps the measures used in the current study placed demands on these same visual stimulus evaluation systems.

Y. Stern et al. (1993) suggested that timed motor tasks, such as those used in this study, are among the more sensitive measures for detecting subtle neuropsychological impairment. As was mentioned previously, the deficits associated with HIV infection are hypothesized to be subcortical in nature. A heterogeneous sample of men with HIV infection showed three general patterns of performance and mood (van Gorp, Hinkin, et al., 1993). One of these patterns consisted of depression, psychomotor slowing, and decreased verbal memory. This pattern is suggestive of a subcortical dementia. Slowed motor speed as shown in the present sample would be consistent with this hypothesis of subcortical dysfunction. In conclusion, decreased performance in the HIV+ group on measures of motor speed is possibly due to some physiological mechanism of the infection in the central nervous system, perhaps affecting subcortical structures. Elucidation of this mechanism remains for future research.

Depression, as mentioned, can be seen in association with subcortical impairment. Harker et al. (1995) observed that if depression is part of the pattern of neurological impairment in individuals with HIV infection, then controlling for this

variable would in essence remove part of the effect one is hoping to describe. These researchers suggest that partialling out the affective component of any mood measure used in a study, but leaving the somatic component in the analysis would be one method of solving this dilemma. In the current study, the SCL-90-R was found to be highly correlated with the Beck Depression Inventory. Thus, if subcortical deficits were evident, it is possible that partialling out the variance accounted for by this measure may have removed some of the effect. However, even when the distress measure was accounted for, decrements in motor speed were still evident, suggesting that neuropsychological measures were still able to detect impairment.

Distress did account for a significant proportion of the variance in one and possibly two cognitive domains (executive function, and to a lesser extent, attention/speed of processing). The observed absolute differences on the SCL-90-R between groups were small and not statistically significant. This is surprising, given the fact that the asymptomatic group is facing a chronic, debilitating disease often associated with a loss of social support and the added burden of a stigma attached to the illness. It was suggested at the beginning of this paper that failures to find differences between groups on measures of distress might be due to the use of strict diagnostic criteria which would only detect obvious psychopathology. Findings by van Gorp, Moore, et al. (1993) suggest that both clinician ratings of distress, as measured by the Hamilton Rating Scales for Depression and Anxiety, and self-reports (such as the BDI and MMPI) are in fact highly correlated. Measures of anxiety were also highly correlated with depression. This might imply that these measures are

detecting general levels of distress, rather than discrete clinical syndromes. It is possible that using the SCL-90-R to detect general distress is not effective. Instead, this measure may only detect specific affective components that previously used measures of depression and anxiety have. Alternatively, perhaps these supposedly more specific instruments were in fact indicating general distress. This might account for the similar findings of this study as compared to those using more objective measures of clinical syndromes.

Studies such as this one have implications for future research that aims to predict cognitive decline in HIV infection. It is important to further characterize the course of the disease so that the success or failure of antiretroviral treatment might be more effectively assessed. Identification of infected persons who will go on to develop significant cognitive decline (e.g., ADC) might also be achieved. To this end, there are few studies currently which examine longitudinal issues. One study by Y. Stern et al. (1993) which followed HIV+, non-AIDS subjects over a two year period found that these patients failed to show the expected practice effects on repeated neuropsychological test measures of motor speed and executive function evidenced in non-HIV subjects. With such little evidence either for or against further cognitive decline in asymptomatic men who show some cognitive decrements, it is clear that questions concerning long-term outcome remain to be answered, and are ripe for further clarification. Longitudinal studies which investigate whether early cognitive decline is predicative of developing dementia would shed light on possible early identification factors. Through identification, implementation of services early in the

disease could be justified, in an effort to offset the effects of future decline, allocate services more efficiently, and perhaps lead to better understanding of the dementing process seen in HIV+ individuals.

It is possible, if not likely, that only a subgroup of asymptomatic HIV+ patients will go on to develop significant cognitive decline. One limitation of the current study is that an examination of mean scores may have obscured individual performances.

The finding that increases in psychological distress did account for a significant part of the variance in measures of executive function and to a lesser extent attention/speed of processing have implications for intervention early in the disease course. As medications to combat the physical side effects of HIV infection are developed, improved, and subsequently extend a patient's life expectancy, the psychological management of this group of chronically ill patients will increase in importance. As HIV is by nature a malfunction of the immune system, it is possible that decreasing stress might simultaneously improve immune functioning. Glaser and Kiecolt-Glaser (1987) proposed the possibility that stressors in the environment might activate the virus (not unlike the herpes virus), resulting in more acute and earlier immune suppression. One study reported benefits of early immunomodulatory interventions such as behavioral interventions and a time-limited aerobic exercise training program (Antoni et al., 1990). They believed that these interventions not only improved cellular and humoral immune functioning, but improved psychological functioning as well. These therapies may restore competence and halt the

progression of this disease. The intervention involving an aerobic exercise regimen was only conducted during the time immediately preceding testing for the HIV virus and the time following the report of a positive blood test. It would be interesting to see if these same benefits are evident at a somewhat later, yet still asymptomatic, stage of infection.

Traditional psychotherapeutic approaches have been recommended, along with the teaching of coping skills, supportive therapy, and peer support groups (Tross & Hirsch, 1988). These same researchers caution against the imprudent use of psychotropic medications, as these can compound physical symptoms. Manly et al. (1995) found that in a sample of HIV+ men, those who relied primarily on approach-avoidant coping mechanisms and had smaller support networks were more cognitively impaired than other men in their group. This subset may be more isolated and find an increased need for expending energy on coping strategies. These might be fruitful areas to target in supportive therapy or peer support groups.

In summary, this sample of asymptomatic HIV+ men experienced slightly more distress than HIV- men, and this disturbance was associated with decreased performance on measures of executive function and, to a lesser extent, attention and concentration. Through increased psychological intervention and support services, which ideally should be available very early in the course of infection, it may be possible to relieve some of this emotional distress. With relief, patients may have greater cognitive energy, allowing them to focus their attention, effectively problem solve, and in general function more effectively. However, it is important to

recognize, as evidenced through decreased motor speed, the possible neurological effects of the presence of HIV in the central nervous system. These markers (i.e., motor speed performance) should be carefully evaluated in an attempt to clarify the natural history of the disease and possibly predict subsequent cognitive and physical decline. With prediction, practical intervention may be possible, with not only the result of possibly improving immune function and extending life expectancy, but also affording patients an opportunity to address their future options and obligations prior to disease progression.

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Appendix - Glossary

ADC - AIDS-Dementia Complex

ARC - Aids-Related Complex; includes physical symptoms of AIDS and decreased immune functioning, but no presence of opportunistic infections

basal ganglia - specific interconnected grey masses deep in the cerebral hemispheres and in the upper brain stem, which are involved in motor coordination

blood-brain-barrier - the selective barrier separating the blood from the parenchyma of the central nervous system

CD4/CD8 counts - counts of lymphocyte cells or white blood corpuscles which aid in immune responses; decreased CD4 counts signify a decrease in immune functioning.

ELISA - Enzyme-Linked Immuno-Sorbant Assay; any enzyme immunoassay using an enzyme-labeled immunoreactant and an immunosorbant

executive function - term used to describe cognitive functions which are measured by tasks requiring, e.g., problem solving, mental flexibility, ability to inhibit impulsive responses, and planning skills

lymphadenopathy - disease of the lymph nodes

psychomotor speed - the rate at which a person can translate mental processes into voluntary muscular movement

opportunistic infection - an or infection caused by a microorganism which does not ordinarily cause disease but becomes pathogenic under certain circumstances

otoneurologic - dealing with those portions of the nervous system related to the ear

seroconversion - the change of a seronegative test from negative to positive, indicating the development of antibodies in response to infection

VITA

Surname: Stroup Given Names: Elizabeth Suzanne

Place of Birth: Canton, Ohio, U.S.A.

Educational Institutions Attended:

University of Victoria	1991 to 1995
Wittenberg University	1986 to 1990

Degrees Awarded:

B.A. Wittenberg University	1990

Honours and Awards:

Graduate Teaching Fellowship	1992-1994
B.A. awarded cum laude	1990
Beta Beta Beta National Biology Honorary	1990
Psi Chi national Psychology Honorary	1989-1990
Lutheran Brotherhood Scholarship	1986-1990
Lutheran Scholar Award	1986-1990
Ohio Board of Regents Scholar	1986-1990

Publications:

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Author: 

Elizabeth Suzanne Stroup
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