Supervisor: Professor Otfried Spreen

ABSTRACT

Documentation of neurological complications and neuropathological findings arising in most AIDS patients has stimulated the need for an investigation of the brain-behaviour relationships associated with human immunodeficiency virus (HIV) infection. This study aimed to verify the hypothesis that a chronic subclinical AIDS dementia exists in view of the neurotropic quality of HIV. Participants were 59 male homosexuals distributed as follows: 17 healthy HIV seronegative, 14 healthy HIV seropositive, 14 AIDS-Related Complex, and 14 AIDS. They were administered a comprehensive battery of neuropsychological tests, including measures of attention, cognition, memory, language, executive, and sensorimotor functions. An examination of the emotional and psychological concomitants was performed using questionnaires of personality (MMPI), anxiety (STAI), and health-related behavioural dysfunction (SIP). Group comparisons were conducted on the basis of Health Status (Healthy vs Nonhealthy) and Medical Diagnosis (HIV-, HIV+, ARC, & AIDS). Results revealed a significant Health Status effect overall, as well as evidence for a deterioration of

higher mental abilities occuring with progression of HIV infection. These findings appear to be independent of the emotional and psychological factors, which are felt to be an integrative part of the AIDS-Dementia Complex (ADC).

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DEDICATION

This dissertation is dedicated to the person who has introduced me to the field of Neuropsychology, Dr. Donald T. Stuss. Over the years, he has proven to be an engaging and motivating employer, an inspiring mentor, and a good friend.

PREFACE

The acquired immune deficiency syndrome (AIDS) is a disorder which attracted the attention of the U.S. medical health community only since the early 1980s. The emergence of this novel epidemic form of immunodeficiency initially stimulated rigorous investigations in the areas of immunology, epidemiology, infectious diseases, and oncology. As the clinical course of the disease progressed, it became apparent that other disciplines could contribute to a better understanding of the unfamiliar ailment. Thus, a review of the literature ultimately included investigations reporting neurological complications, neuroradiological correlates, and neuropathological findings.

Much effort has been invested in research, and the wealth of knowledge being gained has been increasing at an exponential rate, so much so that the results of ongoing studies are often outdated by the time they are published. For this purpose, the review of the background information germane to this study was partitioned as follows: The first chapter provides a brief synopsis of the disease entity. The second chapter focuses on the findings related to the involvement of AIDS in the central nervous system. These two reviews are limited to the state of knowledge available at the outset of this research in order to allow for a better understanding of the rationale and design of the study which are described in chapter three. Chapter four

provides an up-dated review of the more contemporary developments which have been published following the onset of data collection. The methodology and results of this investigation are presented in chapters five and six respectively. The significance of the current observations are discussed in chapter seven, while the last chapter offers suggestions for future research in this area.

CHAPTER ONE

THE ACQUIRED IMMUNE DEFICIENCY SYNDROME

The Appearance of a New Disease

In 1979, an unusual outbreak of cases presenting with *Pneumocystis carinii* pneumonia (PCP), Kaposi's sarcoma (KS), and/or other serious opportunistic infections was observed in young homosexual men without a known underlying immunosuppressive disorder or therapy. The first published report described 5 cases of PCP (Gottlieb, Schroff, Schanker, et al., 1981), followed a month later by another one detailing 26 cases of KS, 5 of which subsequently developed opportunistic infections (4 PCP and 1 toxoplasmosis) (Friedman-Kien, Laubenstein, Marmor, et al., 1981). The Center for Disease Control (CDC) in Atlanta (U.S.) thus formed a task force in order to undertake surveillance of these afflictions (CDC, 1982a). In view of the elusive nature of the putative agent, the CDC defined the new syndrome as follows:

> *"AIDS is characterized by the presence of a reliably diagnosed disease at least moderately indicative of an underlying cellular immune deficiency in a person with no known underlying cause of reduced resistance reported to be associated with that disease."* (CDC, 1982f)

Epidemiology

Recognition and description of the disease constituted the initial phase of the epidemic. Epidemiologic and laboratory investigations focused primarily on the nature and the incidence of AIDS. The disease initially appeared to be circumscribed to a distinct epidemiologically determined segment of the population, i.e. the male homosexual community (Carr, Veitch, Edmond, et al., 1984; CDC, 1982e; CDC, 1982f; Durak, 1981; Ginzburg, 1984; and, Hardy, Allen, Morgan & Curran, 1985). However, other groups at high risk were soon recognized and included parenteral drug abusers (CDC, 1982b; Durak, 1981; Ginzberg, 1984; and, Gopinathan, Laubenstein, Mondale, et al., 1983); Africans (Brun-Vezinet, Rouzioux, Barre-Sinoussi, et al. 1984; Clumeck, Mascaret-Lemone, de Maubeuge, et al., 1983; and, Clumeck, Sonnet, Taelman, et al., 1984); Haitians (Blattner, Kalyanaraman, Robert-Guroff, et al., 1982; CDC, 1982b; Pape, Liauta , Thomas, et al., 1983; Pitchenik, Fischl, Dickinson, et al., 1983; and, Vieira, Frank, Spira, & Landesman, 1983); hemophiliacs (CDC, 1982c; Davis, Horsburgh, Hhasiba, et al. 1983; Elliot, Hoppes, Platt, et al. 1983; and, Kitchen, Barin, Sullivan, et al., 1984;); transfusion-related cases (CDC, 1982d; Curran, Lawrence, Jaffe, et al., 1984; Jett, Kuritsky, Katzmann, & Homburger, 1983; and, O'Duffy & Isles, 1984); female partners and infants of those at risk (CDC, 1982e; CDC, 1983; Harris,

Small, Klein, et al., 1983; Masur, Michelis, Wormser, et al., 1982; Oleske, Minnefor, Cooper Jr., et al., 1983; Pitchenik, Shafron, Glasser, & Spira, 1984; Redfield, Markham, Salahuddin, et al., 1985; and, Scott, Buck, Leterman, et al., 1984); and finally prostitutes (Enlow, 1984; Fauci, Macher, Longo, et al., 1984; Wallace, Downes, Ott, et al., 1983; and, Weiss, Hollander, & Stobo, 1985). Following these observations, AIDS was no longer considered solely as a "gay related immune deficiency (GRID)" syndrome, as was initially postulated (Brennan & Durack, 1981; Britton, Marquardt, Koppel, et al., 1982; and, Horowitz, Benson, Gottlieb, et al., 1982).

Clinical Manifestations

AIDS is characterized by a profound dysfunction of cell-mediated immunity which predisposes a previously healthy individual to contract opportunistic infections (Blattner, et al. 1982; CDC, 1982f; Elkin, Leon, Grenell, & Leeds, 1985; Ginzburg, 1984), or develop neoplasms (Carr, et al., 1984; De Cock, 1984a & 1984b; Ginzburg, 1984). The presenting symptomatology can assume various patterns of expression. The syndromes may present as pulmonary, oncogenic, gastrointestinal, neurologic, or pyrexial (febrile) in nature (Bale, 1984; Black, 1985; Bove, 1984). Typically, AIDS is of insiduous onset. The course of the illness features cumulative deficiencies in the body's cell-

mediated immune mechanisms. Disruption of the immune system leaves the host susceptible to, and, unable to resist infections which are readily stifled and surmounted under normal circumstances. Accordingly, these infections may become life threatening.

Pulmonary. By far, the most prominent lung infection is caused by a protozoon-like ubiquitous organism, *Pneumocystis carinii*, which infects human beings by respiratory route and gives rise to a severe interstitial pneumonia. This infection affects approximately 60% of the AIDS patients. The onset of PCP symptoms is often indolent, progressing over several months, but it may also be fulminant with development of respiratory failure within a few days (Gold & Armstrong, 1984). Chief complaints include nonproductive cough, exertional dyspnoea (shortness of breath), vague chest pains, and fever (National Health Medical Research Council [NHMRC]. 1984). The treatment of PCP is often complicated by aversive reactions to the therapeutic drugs (Gold & Armstrong, 1984). Other sources of opportunistic lung infections are summarized in Table 1.1.

Oncogenic. Approximately 30% of all AIDS patients presents with Kaposi sarcoma (KS). This very rare form of cancer typically affects elderly men (over 60 years of age), often of Mediterranean or Ashkenazi Jewish ancestry, whose immune system has already been suppressed, either by cancer,

Table 1.1

Clinical Manifestations of AIDS

Pulmonary

Pneumocystis carinii
Cytomegalovirus (CMV)
Aspergillus
Cryptococcus
Mycobacterium
Nocardia
Legionella pneumophila

Oncogenic

Kaposi's sarcoma (KS)
Burkitt's lymphoma
Primary non-Hodgkin's B-cell lymphoma (CNS)
Squamous carcinoma (mouth & rectum)

Gastrointestinal

Candida oesophagitis
Cryptosporidiosis
CMV
Salmonellosis
Mycobacterium avium-intracellulare (MAI)
Peri-rectal herpes simplex

Neurological

Primary brain lymphoma
Vascular insults (emboli or vasculitis)
Toxoplasmosis
Cryptococcosis
Progressive multifocal leukoencephalopathy (PML)
Peripheral neuropathy

Pyrexial

CMV
MAI-*scrofulaceum* complex (MAIS)
Mycobacterium tuberculosis
Cryptococcus

chemotherapy, or immunosuppressive drugs administered to inhibit rejection of transplanted organs. The disease is distinctively endemic in Central Africa, where native blacks are far more frequently afflicted than nonblacks, and it shows a strong male predominance, i.e. 10-15 : 1 (Safai, 1984). The classic lesions of KS are multifocal, slow growing violaceous plaques or nodules occurring in the lower extremities. By contrast, the cutaneous lesions in the epidemic or AIDS-related KS tend to be smaller, paler, and have a predilection for the upper trunk, head, and neck areas. Also characteristic of the epidemic form of KS is the fact that the violaceous plaques and nodules may disseminate to mucous membranes (e.g. mouth), to lymph nodes, and/or to the gastrointestinal tract (the most common extracutaneous site). The course of the sarcoma is more chronic and indolent in the older patients and Africans (Safai, 1984). It is moderately aggressive in renal transplant recipients (Harwood, Osoba, Hofstader, et al., 1979), while being more invasive in the epidemic cases with dissemination and rapid spread. In the latter, survival is thus far reported to be 18 months; however, the patient's death is rarely due to the dissemination of the sarcoma, but more often to superimposed development of opportunistic infections. KS affecting young homosexual men appears to be less responsive to chemotherapy (Cole, 1984). Seven percent of AIDS patients develop both KS and PCP (NHMRC, 1984).

Other types of malignant diseases reported in association with AIDS are listed in Table 1.1 (page 7).

Gastrointestinal. Patients presenting with the gastrointestinal syndrome typically suffer from low-volume diarrhea, weight loss, variable degrees of abdominal discomfort and pain (Gottlieb, 1984; NHRMC, 1984). In some cases, the patients appear to suffer from a terminal malignant disease in view of the more profuse diarrhea, unremitting malabsorption, profound weight loss, and cachexia (chronic lack of nutrition and wasting). The pathogens responsible for the most frequent gastrointestinal complications arising with AIDS are presented in Table 1.1 (page 7). In some of the infections, there is no effective treatment, while in others, there is a relapse when treatment is halted, as the abnormality in T-cell function impedes thorough elimination of the organisms.

Neurological. Central nervous system (CNS) manifestations of AIDS are due to infections of various aetiology (viral and nonviral), primary brain tumours (lymphomas), and vascular insults resulting from emboli or vasculitis (Simpson, Snider, Nielsen, et al., 1984). Other neurological complications include toxoplasmosis, progressive multifocal leukoencephalopathy, and painful peripheral neuropathy of unknown aetiology. Opportunistic infections of the CNS may display diffuse or focal characteristics (Gottlieb, 1984). The clinical spectrum

features headaches, personality or cognitive changes, dementia, altered level of consciousness, convulsions, and focal sensory or motor disorders, depending upon whether the meninges, the cortex, the brainstem, or the spinal cord is affected (Gold & Armstrong, 1984; NHMRC, 1984). The various aspects of CNS involvement in AIDS will be discussed at greater length in the following chapter.

Pyrexial. AIDS patients frequently present with the primary symptomatology of high swinging fevers, often of unclear origin (Greene & Slepian, 1984). In the absence of pulmonary, gastrointestinal, and CNS involvement, the infectious agent will most likely be cytomegalovirus or more importantly, widespread *Mycobacterium avium-intracellulare-scrofulaceum* (MAIS) complex. Other organisms responsible for the febrile onset include *Mycobacterium tuberculosis* or *Cryptococcus* (Greene & Slepian, 1984). Enlarged lymph nodes are usually the principal characteristic feature of the pyremic syndrome. The use of antituberculous drugs for treatment of MAIS infections has proven to be largely ineffectual (Brandt, 1984).

The Cause of AIDS

The putative agent responsible for AIDS is a retrovirus, currently referred to as HIV (human immunodeficiency virus) (Marx, 1986). The new denomination supplanted several previous designations of the pathogen.

The dissension over this viral nomenclature stems from the ongoing debate as to who should get priority for uncovering the AIDS virus. Montagnier and his colleagues at the Pasteur Institute in Paris initially named it lymphadenopathy-associated virus (LAV), or immune deficiency associated virus (IDVA) in patients without full-blown AIDS (Montagnier, Dauguet, Axler, et al., 1984). Robert Gallo and his associates at the National Cancer Institute (U.S.) selected human T-lymphotropic virus type III (HTLV-III) (Gallo, Salahuddin, Popovic, et al., 1984). Finally, Jay Levy and his fellow workers at the University of California School of Medicine in San Francisco used the term AIDS-associated retrovirus (ARV) (Levy, Hoffman, Kramer, et al., 1984).

HIV is a retrovirus (RNA tumour virus) of the human T-cell leukemia virus family (HTLV) because of its selective predilection for tropism of lymphocytes (Gallo, 1984). Retroviruses were discovered only in the late 1970s, and are designated as such because they bear an enzyme called reverse transcriptase which allows the synthesis of a DNA copy from their RNA genome. The DNA copy can then be integrated into the genome of the cell i.e. the virus incorporates its own genes to the cell's genes, thus speeding up their own reproduction. This form of genetic transmission goes against the classic notion which

stipulates that genetic transfer is unidirectional, i.e. from DNA to RNA (Marwick, 1984).

Immunologic Abnormalities

The retroviral infection discriminantly impairs an essential unit of the immune system, the T-lymphocytes. Overall, a reduction in the lymphocyte count (lymphopenia) is noted. More specifically, there is a severe depletion of the T-helper (also known as T4) lymphocyte cell, while the number of T-suppressor (also known as T8) cells may be relatively stable or show a relative increment, thus producing a decrease of the normal T4:T8 ratio of the T-lymphocyte subset cell population. Also characteristic of the syndrome is a hyperactivity (proliferation) or dysfunction of the B-lymphocyte cells, and a decrease in cytotoxic responses from the natural killer cells (Fauci, et al., 1984; Lane, Masur, Edgar, et al., 1983; Masur, et al., 1981; Nicholson, McDougal, Spira, et al., 1984; Seligman, Chess, Fahey, et al., 1984).

Other AIDS-Related Illnesses

Two additional prominent syndromes have been witnessed concurrently with the emergence of AIDS: persistent generalized lymphadenopathy (PGL) and AIDS-Related Complex (ARC). Epidemiological similarities between AIDS, ARC, and PGL have been noted: a median age of onset in the 30s; use

of recreational drugs; as well as, frequent histories of multiple sexual partners and sexually transmitted diseases (Cohen, 1984; Fauci et al., 1984).

The principal clinical manifestation of PGL features unexplained persistent (or progressive) swelling of the lymph nodes, particularly in the cervical and axillary areas. The CDC defined it as follows:

> "*(1) lymphadenopathy of at least 3 months duration involving at least 2 sites other than the groin, without evidence of an illness or drug use known to cause lymphadenopathy; and*
>
> *(2) the presence of increased lymph node activity (reactive hyperplasia) as diagnosed by a lymph node biopsy.*" (Lang, Spiegel, & Strigle, 1985; p.13)

The syndrome is also known as lymphadenopathy syndrome (LAS), extended lymphadenopathy syndrome (ELAS), or lymph node syndrome (LNS). The connection between PGL and AIDS remains to be eludicated. Many homosexual men have been known to harbor PGL for many years and not developed AIDS.

In the second syndrome, ARC, constitutional signs and symptoms occur in various combinations with lymphadenopathy, but in the absence of an opportunistic infection or KS. They include fever, prolongued fatigue, malaise, night sweats, weight loss, anorexia, oral candidiasis, spleenomegaly, diarrhea, and minor mucocutaneous infections (tinea or ringworm, warts, herpes simplex) (Mathur-Wagh,

Enlow, Spigland, et al., 1984; Seligmann, et al., 1984). The configurations of symptoms seen in ARC appear to represent parts of the full clinical spectrum seen in AIDS. Furthermore, the syndrome displays a clear affiliation for lymphocytopathic retroviruses and antibodies as demonstrated by serological studies (Popovic, Sarngadharan, Read, & Gallo, 1984; Sarngadharan, Popovic, Bruch, et al., 1984). Therefore, it has been postulated that ARC represents a prodromal stage to AIDS in some patients, and is as such often referred to as pre-AIDS. Prospective studies suggested that between 5 and 19% of patients with PGL and/or ARC eventually progress to full-blown AIDS (Brynes, Chan, Spira, et al., 1983; Mathur-Wagh et al., 1984; Metroka, Cunningham-Rundles, Pollack, et al., 1983). On the other hand, not all AIDS cases go through an identifiable prodrome. In view of this, another hypothesis stipulated that PGL and ARC represent alternative responses to infection with HIV, either a milder form of AIDS, or possibly a more competent immune system coping with the infectious pathogen (Cheingsong-Popov, Weiss, Dalgleish, et al., 1984).

PGL and ARC patients display a spectrum of immunological findings ranging from completely normal to one similar to those seen in AIDS patients (NHMRC, 1984). A triad of constitutional signs, such as night sweats, spleenomegaly, and leukopenia (reduction of white blood

cells), has especially been associated with a poor prognosis, i.e. progression to full-blown AIDS (Mathur-Wagh, et al., 1984).

CHAPTER TWO

AIDS AND THE CENTRAL NERVOUS SYSTEM

Neurological Complications

In view of the nature of the cell-mediated immune regulation, susceptibility to specific infections can be predicted. Immunocompromised patients are especially pregnable to viruses (Miller, Barrett, Britton, et al., 1982; Siegal, Lopez, Hammer, et al., 1981), fungi (Gottlieb et al., 1981), mycobacteria (Greene, Sidhu, Lewin, et al., 1982), and parasites (Follansbee, Busch, Wofsy, et al., 1982; Gottlieb et al., 1981; Masur, Michelis, Greene, et al., 1981). Intact cell-mediated immunity is necessary to stifle these agents. In comparison to other organ systems, the CNS mounts less cellular immune response (Chernik, Armstrong, & Posner, 1973; Horowitz, et al., 1982), and is consequently more susceptible to infections caused by cytomegalovirus (CMV), *Toxoplasma gondii*, *Cryptococcus*, papovavirus and *Mycobacterium avium-intracellulare* (Snider, Simpson, Nielsen, et al., 1983). Before the advent of AIDS, a whole clinical spectrum of CNS disease had been well documented in immunosuppressed patients due to organ transplant, cancer, Hodgkins, and non-Hodgkins lymphoma, chronic lymphocytic leukemia, or longlasting steroid therapy (Chernik et al., 1973; Horowitz et al., 1982; Ruskin & Remington, 1976). Similarly, primary lymphomas of the CNS

are rarely encountered in the immune competent host, but have been reported in immunocompromised patients with Wiskott-Aldrich syndrome, or disorders stemming from organ transplant (CDC, 1982a; Filipovich, Spector, & Kersey, 1980; Pitchenik, et al., 1983a; Schneck, & Penn, 1971; Snider, Simpson, Aronyk, & Nielsen, 1983).

Initially, scant attention had been given to the neurologic manifestations accompanying AIDS. A number of studies have since documented the emergence of neurologic complications arising with HIV infection (Grenell, Small, Harris, et al., 1983; Kaminsky, Mathur, Yancovitz, et al., 1983; Koppel, Wormser, Tuchman, et al., 1985; Luft, Brooks, Conley, et al., 1984; Snider, et al., 1983b), and reported occurrence rates ranging from 30% to 75% of cases (Bredesen & Messing, 1983; Elkin, et al., 1985; Gapen, 1982; Levy, Bredesen, & Rosenblum, 1985; Simpson, Snider, Nielsen, et al., 1983; Snider et al., 1983a; Snider et al, 1983b). The neurological complications transpiring with AIDS are quite diverse and may present as the principal feature of the syndrome in 10% of all AIDS cases (Levy et al., 1985; Moskowitz, Hensley, Chan, et al., 1984), and in 43% of Haitian patients (Pitchenik, et al., 1983a; Vieira, Frank, Spira, & Landesman, 1983). They may emerge at any stage of the disease process (Gapen, 1982), or were the cause of death (Britton, et al., 1982; Gopinathan, et al., 1983; Herman, 1983; Hooper, Pruitt, & Rubin, 1982).

Infectious agents akin to those seen in immunosuppressed patients have been associated with the neurologic complications arising in AIDS. Thus, infections caused by viruses, fungi, and protozoa commonly include CMV (Reichert, O'Leary, Levens, et al., 1983), *Cryptococcus neoformans* (Whelan, Krischeff, Handler, et al., 1983), *Aspergillus fumigatus* (Gapen, 1982), *Toxoplasma gondii* (Whelan et al, 1983), papovavirus (Bedri, Weinstein, & De Gregorio, 1983), *Candida algicans* (Snider et al., 1983b), *Mycobacterium tuberculosis* (Pitchenik, Fischl, & Walls, 1983), and *Mycobacterium avium-intracellulare* (Snider et al., 1983b). As well, intracranial malignant mass lesions develop in some AIDS patients (Hauser, Luft, Conley, & Remington, 1982; Pitchenik et al., 1983a; Scott, et al., 1984). The neoplastic processes usually witnessed consist of primary CNS lymphoma (of the B-cell typology), systemic malignancies metastasizing to the brain, and plasmacytoma (Snider et al., 1983b). The immunological abnormality is thought to cause particular proclivity for the B-cell neoplasms in the CNS (Hasek, Chutna, Sladecek, & Lodin, 1977).

The wide spectrum of clinical neurological complications reported were classified on the basis of the following: 1) the distinct syndromes/diseases (Table 2.1); 2) the specific neuropathological features; and/or 3) the general pattern of neurological involvement (focal vs

Table 2.1

CNS Complications of HIV Infection

Viral Syndromes

Subacute encephalitis
Atypical aseptic meningitis
Herpes simplex encephalitis
Progressive multifocal leukoencephalopathy
Viral myellitis
Varicella-zoster encephalitis

Non-viral infections

Toxoplasma gondii
Cryptococcus neoformans
Candida albicans
Coccidioidomycosis
Treponema pallidum
Atypical mycobacteria
Mycobacterium tuberculosis
Aspergillus fumigatus
Escherichia coli bacterium

Neoplasms

Primary CNS lymphoma
Systemic lymphoma with CNS involvement
Kaposi's sarcoma

Cerebrovascular accident

Infarction
Hemorrhage
Vasculitis

nonfocal, or functional vs organic). Although *Pneumocystis carinii* is the most frequent source of opportunistic infection in this patient population, it has not been documented in CNS involvement (Kelly & Brant-Zawadzki, 1983). Similarly, dissemination of Kaposi's sarcoma to nearly all organ systems has been documented extensively (Gorin, Bale, Halks-Miller, & Schwartz, 1985); however CNS involvement or metastasis has been rare (Gorin et al, 1985; Levy, Pons, & Rosenblum, 1984). Treatment is available for most of the neurological complications that are a result of opportunistic infections (see Bredesen & Messing, 1983; Gorin et al., 1985; Gottlieb et al., 1981; Loewenstein & Sharfstein, 1983-84 for a review). However, these therapeutic measures have been more successful in the immunosuppressed patients due to causes other than AIDS (Armstrong, 1984).

Of the syndromes listed in Table 2.1 (page 20), one is of particular interest, and occurs in about one third of the AIDS victims (Nielsen, Petito, Urmacher, & Posner, 1984). Subacute encephalitis was the term initially used to refer to the most prevailing neurological syndrome (of viral aetiology) encountered in the AIDS patient population (Gapen, 1982; Snider et al., 1983b). More recently, the syndrome has been designated as the AIDS-dementia complex (Navia, Jordan, & Price, 1986). Generally, the syndrome consists of a progressive, subcortical-type, dementia which

is often accompanied by focal motor deficits, signs of frontal lobe damage (such as frontal release signs), headaches, seizures or hemianopsia (Levy et al., 1985; Snider et al., 1983b). The clinical manifestation typically begins with a confusional state or subtle cognitive changes associated with fever, malaise or mild metabolic disturbances (Snider et al., 1983b). Difficulty with concentration and memory loss, withdrawal from occupational and social situations, and loss of sexual drive list among the early complaints (Jordan, Navia, Petito, et al, 1985). Profound psychomotor retardation also mimic the semblance of psychological depression. The early behavioral variations are often interpreted to reflect nonspecific decline or depression (Snider et al., 1983b), particularly when they arise in patients suffering from pulmonary infections or multiple metabolic abnormalities. However, the systemic diseases were considered sufficient to explain the neurological picture in only a limited number of patients presenting with subacute encephalitis (Snider et al., 1983b). The syndrome is progressive and extends over the course of several months. Nonspecific clinical manifestations, except for occasional seizures, are consistent with the diffuse distribution of the neuropathology (Jordan et al., 1985b). Deterioration progresses to profound dementia often associated with confusion and incontinence. The patients are usually

bedridden at this stage and endure recurrent infections resulting in death (Snider et al., 1983b). Symptomatic remission rarely occurs and no treatment has proven effective. Although subacute encephalitis is directly associated with death in only a few cases, morbidity is high in view of the severe intellectual and social deterioration that occurs in the later stages of the syndrome.

The AIDS patient population may suffer a progressive cerebral disorder even before the CNS dysfunction becomes clinically apparent (Hoffman, 1984). Kermani and his colleagues suggested that organicity is part of the natural history of AIDS (Kermani, Drob & Alpert, 1984). It has also been hypothesized that a chronic AIDS encephalopathy exist in view of the neurotropic quality of HIV, (Shaw, Harper, Hahn, et al., 1985). Also supporting this contention, reports of slow alpha basal activity (8-9 Hz) on the EEG have been noted in 50% (13 of 26) of male homosexuals with AIDS or ARC, a percentage much higher than the 10-15% typically found in normal adults (Enzensberger, Fischer, Helm & Stille, 1985). In this series, acute or subacute encephalitis subsequently developed in 38% (5 of 13) of cases displaying atypical EEG patterns. The remaining 8 patients showed persistent slow alpha basal activity together with mild organic "psycho-syndrome", which was interpreted as indications that they were perhaps harboring a chronic subclinical encephalopathy due to the AIDS virus

(Enzensberger et al., 1985). These findings point to the need for electroencephalography (EEG) as a regular part of the diagnostic protocol in patients with AIDS or ARC. The procedure appears to provide helpful information regarding the initial manifestations of encephalopathy, and perhaps preceding the onset of clinical appearance. The combination of EEG and neuropsychological tests was also recommended for early CNS detection (Enzensberger et al., 1985).

Furthermore, reports were documenting that HIV may infiltrate the brain without affecting the immune system (Ho, Rota, Schooley, et al., 1985). In a series of nine healthy homosexual men demonstrating HIV antibodies and no immunological abnormalities, several patients revealed signs of CNS dysfunction while 2 patients developed dementia, 2 others with no neurological signs at the outset suffered an acute meningitis, and 1 died (cause of death not specified) (Meer, 1986). Although the underlying mechanism is not fully understood, the findings suggested that some AIDS patients showed immunological dysfunction, others revealed CNS deterioration, while others suffered from both (Meer, 1986). Presumably, both AIDS and ARC patients need to be monitored for signs of mental dysfunction in addition to the emotional symptoms when facing the fatal disease. Although the entire range of the AIDS population may develop neuropathy, those harboring a history of opportunistic infections (particularly PCP) appear to be at greatest risk

as compared to those presenting with KS only (Snider et al., 1983b). This finding is thought to reflect the observation that patients with opportunistic infections tend to reveal a more profound degree of immunological dysfunction (Snider et al., 1983b).

Isolations of HIV from CSF, brain, spinal cord and/or peripheral nerve were recovered in 73% of patients with AIDS related neurologic syndromes, suggesting that the retrovirus was not only lymphotropic in nature, but also had a neurotropic quality (Ho et al., 1985; Resnick, diMarzo-Veronese, Schupbach, et al., 1985). Thus, HIV must now be included to the list of viruses that can either thrive in the brain without causing clinical diseases, or can directly engender a chronic progressive neurologic disorder (Black, 1985; Resnick et al., 1985). It appears that lymphocytes may pass through the blood-brain-barrier and penetrate the CNS without causing apparent lesions to the brain (Fournier, Tardieu, Lebon, et al., 1985). Presumably, the HIV virus may be carried to the brain by infected lymphocytes (T-cell) in this way. As yet, the incubation period of AIDS encephalopathy is unknown. It is also believed that HIV may retreat into the brain cells for indefinite periods of time and re-infiltrate the blood stream to assail the immune system ad lib (World Health Organization [WHO] Chronical, 1985).

Neuroradiologic Features

The CT scan of AIDS patients with neurological complications can display mild to severe generalized cortical atrophy (Bursztyn, Lee & Bauman, 1984; Snider et al., 1983b). However, the inability to mount an appropriate immune response may alter CT patterns as compared to those in immune competent hosts (Elkin et al., 1985; Kelly & Brant-Zawadzki, 1983), and render the differential distinction between two neuropathological processes more problematic (Kelly & Brant-Zawadzki, 1983). While some patients fail to demonstrate CT abnormality concurrently with the onset of neurological signs and/or symptoms, many others show altered or atypical CT representations. Thus, in some instances of AIDS, patients develop neurological complications and progressive deterioration, yet repeated CT scans fail to reveal abnormalities; for example, two cases presented in the literature did not show CT findings until 6 weeks (Bernick & Gregorios, 1984) and 4.5 months (Milligan, Katz, Craven, et al., 1984) after the onset of the illness, respectively. Mortality from CNS complications may greatly increase in the absence of diagnostic measures. Normal CT scans have been observed in the context of intracerebral toxoplasma diagnosed from notable increases in titers and significant improvement following therapy (Handler, Ho, Whelan & Budzilovich, 1983). In contrast, neuroradiological procedures may also prove useful as prognostic indicators.

For example, CT examination performed on a patient suffering from isolated fevers during 5 weeks and without other neurological manifestations, revealed an intracerebral mass in the occipital lobe, and toxoplasma encephalitis was suspected (Roue, Debord, Denamur, et al., 1984).

Early investigations suggested that the lack of significant or diagnostic serological test titers, typical of the AIDS patient, resulted from the immune deficiency; the majority failed to mount antibody responses to antigen stimulation (Meer, 1986). Often, no consistent relationship between the development of neuropathology and the results of serological analyses can be found (Levy, Pons & Rosenblum, 1983; Snider, et al., 1983a). Since the various possible etiologies require distinct therapies, equivocal or nondiscrete diagnostic findings of CT scans, CSF, and serologic examination all contribute to make therapeutic management difficult in these patients (Chan, Moskowitz, Olivella, et al., 1983; Luft, Conley & Remington, et al., 1983; Post, Chan, Hensley, et al., 1983). Tissue examination by means of a biopsy is essentially the only sure method of lesion diagnosis before death. However, the use of magnetic resonance imaging (MRI) has proven more revealing in the more recent studies. De la Paz and Enzmann (1988) reviewed the literature which compared the results of MRI and CT examinations, and found that the MRI was notably more sensitive than the CT in detecting abnormalities. Post

and his associates have recommended the use of MRI in patients who present with clinical evidence of encephalitis but fail to show discrete lesions on the CT scan (Post, Sheldon, Hensley, et al., 1986). The superior resolution and sensitivity of the MRI has been especially observed in cases of white matter lesions (Post et al., 1986).

Neuropathological Correlates

The underlying pathology of HIV infection is best described by the different processes involved and may be classified into 3 types: infectious, neoplastic and degenerative. Autopsy findings reveal diffuse pathology characteristic of viral invasion and involve both grey and white matter throughout the CNS. Neuropathological features include scattered glial nodules, more frequent in grey than white matter, associated with enlarged cells containing intranuclear inclusion bodies, neuronal loss, microscopic foci of demyelination, Alzheimer type II cells, and no evidence of an inflammatory response (Bursztyn et al., 1984; Gapen, 1982; Jordan et al., 1985b; Nielsen, Urmacher & Petito, 1983). Initially, precise etiology remained elusive and suggested focal or generalized CMV or *Toxoplasma gondii* infection (Snider et al., 1983b). Because of the pathological similarity between CMV encephalitis reported in renal transplant recipients (Bale, 1984; Dorfman, 1973; Schneck & Penn, 1971) and AIDS subacute encephalitis, it was

postulated that the herpes virus may be the pathogen involved. However, brain cultures from AIDS patients with subacute encephalitis have either produced diverse pathologies or failed to grow (Levy et al., 1985). Furthermore, CMV antigens have been detected in only a small number of the glial nodules and not found outside the inclusion-bearing cells (Jordan et al., 1985b). The scarcity of CMV isolation contrasts significantly with the widespread pathological changes. HIV has been isolated in the brain and spinal cord of AIDS patient (Ho, et al., 1985; Shaw et al., 1985) and appears to be the putative agent responsible for such a syndrome (Ho et al., 1985; Meer, 1986). Thus, it was concluded that CMV was another concurrent infection and not aetiologically associated to the neuropathology observed (Ho et al., 1985; Jordan et al, 1985b).

Considerably more extensive pathological changes have been observed at autopsy in contrast to the degree of atrophy depicted on CT examination (Bursztyn et al., 1984). It was suggested that a greater percentage of the AIDS population suffer from subacute or chronic viral infections of the brain than what is actually detected (Koppel, et al., 1985). A systematic comparison of premortem diagnoses to postmortem findings undertaken in a small sample (n=12) of AIDS patients revealed that 75% of the patients had suffered clinically undiagnosed infections and malignancies,

including one CNS neoplastic lymphoma (Hui, Koss & Meyer, 1984). This illustrates the importance of postmortem investigations in victims of AIDS. The finding also suggests that AIDS patients tend to be underdiagnosed rather than misdiagnosed. In the forementioned study (Hui et al., 1984), the length of time between premortem and postmortem findings (2 weeks to 8 months) might have been a significant factor in the sequential development of infections. However, another study also supports more widespread CNS involvement at autopsy as compared to CT measures with only 2 to 6 days time interval (Post et al., 1983). Additional studies have corroborated such findings (Levy, et al., 1984; Snider et al., 1983b). Thus, unexpected postmortem findings occur in a number of patients who either fail to show neurological signs of symptoms, or reveal findings additional to those expected from the neurological manifestations (Jordan et al., 1985b; Levy et al., 1985; Levy et al., 1984; Snider et al., 1983b).

In an attempt to document the frequency and histopathologic characteristics of the various neurological manifestations associated with AIDS, autopsies of AIDS victims were performed in 52 consecutive cases (Moskowitz et al., 1984). Neuropathologic features were detected in 73% of the sample. Grossly visible lesions appeared in 56% of the patients, while microscopic analyses revealed neuropathology in all other cases. No significant

neuropathologic findings were detected in 27% of the patients. However, the authors suggested that with more sophisticated methods, the spectrum of neuropathological findings could conceivably be expanded. The proximate cause of death was due to the CNS complications in 29% of the patients, toxoplasma encephalitis being the most prominent determinant. Some cases of cerebral toxoplasma examined at autopsy have also failed to reveal evidence of continued active protozoan infection or any other pathogen consistent with the degree of tissue deterioration observed (Handler et al., 1983).

Neuropsychiatric Manifestations

Inattention and misdiagnosis in early cases have resulted in a failure to recognize the neuropsychiatric signs that are now being documented in the literature (e.g. see Loewenstein & Sharfstein, 1983-84; Perry & Jacobsen, 1986). Psychiatric disorders associated with HIV infection have in some instances preceded the symptoms of immunological nature (Britton & Miller, 1984; Hoffman, 1984; Perry & Jacobsen, 1986). The new understanding that HIV could directly affect the CNS and produce neurological symptoms, and the high percentage of postmortem findings involving the brain, lead to a reexamination of psychiatric symptoms occuring with AIDS. Initially, psychiatric complications were attributed to psychological (functional)

reactions to acquiring the deadly and socially stigmatizing disease. However, recognition of other factors also suggested that the symptoms may be organic in origin. Firstly, AIDS and ARC patients often suffered some degree of lethargy, apathy, and other unexplicable and elusive psychiatric disturbances, before (weeks, months, or years) developing prodromal signs of the syndrome. Secondly, an unusually high incidence of severe psychiatric disorders was occurring in individuals with no premorbid history of serious personal or familial maladjustment (Perry & Jacobsen, 1986). A review of case studies reported in the literature intimated that the neuropsychiatric presentation of AIDS and its related syndromes simulated various functional psychiatric disturbances (Perry & Jacobsen, 1986). For example, paranoid psychosis, hallucination, as well as depression associated with extreme withdrawal and severe anxiety listed among the reported observations (Britton, et al., 1982). A particular triad of psychiatric symptoms was reported in three AIDS victims: mood disturbance, thought disorder with grandiose delusions, and profound memory deficits (Kermani et al., 1984). Since previous psychiatric history and emotional reaction to the medical illness could not adequately explain the last two symptoms, organic impairment was considered a viable explanation. The psychotic manifestation encountered in some AIDS patients was thought to be neurologic in nature,

and to result from the AIDS pathogen in the brain or from undiagnosed intracerebral viral infections (Miller, et al., 1982).

Overall, the whole spectrum of clinical manifestations may be summarized under two broad denominations of psychiatric features: a mild chronic depression, and an acute psychosis (Perry & Jacobsen, 1986). Characteristic symptoms of both these syndromes are outlined in Table 2.2. Mental disorders associated with AIDS are said to be "typically atypical" (Perry & Jacobsen, 1986, p.140), i.e. they do not always correspond to the standard diagnostic syndromes. AIDS patients who are presently assessed for the purpose of establishing their mental status are those referred to a psychiatric consultation liaison-service. Patients are examined to distinguish functional disorders from dementia, to evaluate depression, or anxiety and depression, and verify acute delirium (Dilley, Ochitill, Perl & Volberding, 1985). Early impairment caused by HIV infection was found to be quite subtle, mild or asymptomatic, and may go undetected by the standard mental status examination (Perry & Jacobsen, 1986). A more in depth examination or neuropsychological assessment may be necessary to uncover the subtle deficits.

A psychological study carried out at University of California in Los Angeles revealed that AIDS patients displayed a degree of distress ranging midway between normal

Table 2.2

Characteristic Symptoms of Mild Chronic Depression and Acute Psychosis Seen in AIDS

Mild Chronic Depression	Acute Psychosis
Onset:	
More often gradual but may be acute	More often acute
Symptoms:	
Dysphoric mood	Grandiosity
Apathy	Suspiciousness
Extreme passivity	Delusional thinking
Social withdrawal	Hallucinations
Generalized weakness	Psychomotor retardation
Fatigue	Rambling & repetitive speech
Anorexia	Confusion
Hypersomnia	Blunted affect
Complaints:	
Forgetfullness	
Impaired concentration	
Cognitive deficits:	
Subtle to incapacitating	Subtle to incapacitating
DSM-III Diagnosis:	
Major depression	Schizophrenic disorder
Dysthimic disorder	Acute paranoid disorder
Adjustment reaction with depressed or anxious mood	Brief reactive psychosis
	Mania
	Major depression with psychotic features
Presentation:	
	Usually as part of a severe medical episode
	Frequently anteceded/replaced by the depression-like symptoms

(Perry & Jacobsen, 1986)

college males and male psychiatric outpatients (Wellisch, 1985). Fatigue and anger subscales of the POMS (Profile of Mood States) were the only subscales on which they surpassed the psychiatric outpatients. Furthermore, the AIDS patients appeared to be clearly aware of their emotional distress.

Neuropsychological Investigations

At the time of this study (1986-87), only a few observations concerning the cognitive aspects of AIDS patients were available. Typically, they have been referenced in a more general discussion of neurological implications, in the form of abstracts, or as medical news updates. For example, Meer (1986) announced that a severe impairment for completion of timed tasks, complex problem solving, and short term memory was found in 50% of AIDS victims (n = 23) who were presenting complaints of headaches or depression. He compared these findings to the ones from AIDS patients (n = 26) showing no apparant signs of neurological problems. In this latter sample, 85% displayed delayed response time in tasks of visual and motor abilities. Only four patients had been diagnosed as depressed. The authors felt confident that the deficits reflected an early manifestation of debilitation or dementia.

In another series, dementia appeared as the initial manifestation in nine patients who were subsequently

diagnosed as having AIDS (Tross, Holland, Wetzler, et al., 1985). Cognitive impairment occurred in 50% of AIDS patients (n = 180) manifestating neurological complications over a period of three years (Tross et al., 1985). The clinical course typically revealed deterioration over several months, however, the progression of symptoms can be more abrupt and develop over a period of weeks. A distinct longitudinal study examined AIDS patients (n = 22) without documented neurologic dysfunction at the inception of the investigation, and indicated that 82% revealed cognitive impairment. Memory, language, and reasoning abilities were primarily affected; one to seven functional areas were found impaired (Holland & Tross, 1985).

As mentioned previously, these reports are only brief and do not provide a qualitative analysis of the impairments observed in the cited functional areas. Also, no studies had before the onset of this study in 1985, systematically investigated the level of cognitive function of the fatally affected AIDS patients in comparison to other similarly ill groups. Although emotional aspects have been considered as possible underlying factors resulting in neurological manifestations, little attention has been focused on the effects of multiple recurrent systemic diseases, or their therapeutic management on the level of intellectual functioning.

CHAPTER THREE

THE PROPOSED INVESTIGATION

Rationale

On the basis of clinical experience and neuropathological findings, it appears that neurologic manifestations arise in most AIDS patients (Jordan, Navia, Cho, et al., 1985; Tross et al., 1985). These neurological signs are often subtle, and do not always intimate the underlying nature of the disease. Therefore, they may be easily overlooked given the devastating character of the illness (Gapen, 1982). Not suprisingly, most AIDS patients become depressed when they are diagnosed, and their depression may conceal a more profound problem.

Holland and Tross (1985) observed that AIDS dementia was indiscernable from depression and suggested that neuropsychological testing be undertaken for the purpose of differential diagnosis. Forgetfulness, poor concentration, loss of interest in work, loss of libido, apathy or blunted affect, psychomotor retardation and withdrawal list as the early signs of the dementia/encephalopathy associated with AIDS (Holland & Tross, 1985; Shaw et al., 1985; Snider et al., 983b). However, such symptoms are often present in functional disorders such as depression. Symptoms occuring in the later phases are more neurological in nature and include confusion, disorientation, seizures, myoclonus,

mutism, decreased mentation, and coma. Possible gait disturbances, ataxia, and paraparesis have also been noted (Holland & Tross, 1985; Shaw et al., 1985; Snider et al., 1983b).

Subtle changes in patients may be easily missed, and may require the following factors for proper identification: i) familiarity regarding the premorbid personality of these patients, ii) attentive serial examinations, iii) the awareness of the potential neurological morbidity, and iv) the proper knowledge to recognize the organic signs. Slight and nonspecific fluctuation in alertness, mood, personality and reasoning skills are often associated with fevers, metabolic perturbation, and reactive depression, or other psychological factors (Koppel et al., 1985). On the other hand, they may be altogether dismissed without further quest.

The emergence of this novel epidemic form of immunodeficiency has puzzled the medical field as much by its overwhelming nature, its fatality, its retroviral etiology, and its rapid spread in some communities, as by the absence of effective treatment to date. Although the new clinical entity and its parent syndromes have stimulated a plethora of research investigations, examination of the neuropsychological aspects of AIDS has only recently started and awaits systematic documentation. Neuropsychological assessments may alert physicians to the presence of CNS

dysfunction when other diagnostic measures prove to be nonindicative, and may thus help identify patients at the initial phase of the neurologic dysfunction when treatment may prove critical to outcome. Early evaluations of AIDS patients who are neurologically asymptomatic can also provide baseline measures for comparisons in follow-up studies. Furthermore, the nature of the cognitive deficits seen in the AIDS dementia must be evaluated in order to differentiate them from depression and anxiety, as well as from other neurological complications arising in this patient population. The major thrust of the proposed study is thus concerned with the brain-behaviour relationships associated with HIV infection.

The initial step in understanding the disease has been to describe the clinical/systemic manifestations, the epidemiologic distribution, the mode of transmission, the immunologic dysregulations, and more recently, the neurologic complications. Analogously, the overall objective of this study is descriptive in nature and seeks to present a profile of the intact and compromised neuropsychological functions that are characteristic of the HIV infected victim. Toward this end, a battery of tests was used to assess all major functional areas including attention, concentration, memory, language, reasoning abilities, as well as motor and sensory functions. Crucial factors associated with AIDS, such as depression, anxiety,

and psychological adjustment, may seriously affect the neuropsychological profile and were therefore evaluated as well. Both psychological and neuropsychological profiles displayed by the AIDS patients should be compared with those manifested by a control population of healthy homosexuals, one group testing negative for HIV antibodies, and one group testing positive. The sero-negative group was used to provide validation of the neuropsychological tests as normative data cannot be used in view of the highly selected population involved here. These control groups are similar to the study sample with respect to demographic, clinical, and lifestyle characteristics.

The susceptibility of the AIDS victims to harbor opportunistic CNS infections or malignancies has been well recognized. In an attempt to document the association of cerebral function/dysfunction with the AIDS pathogen per se, as opposed to secondary disease processes, only neurologically asymptomatic AIDS patients have been sampled. The study may therefore provide supportive evidence for the postulated subclinical chronic encephalopathy induced by the AIDS virus (Canadian Disease Weekly Report, 1986b).

In order to provide a neuropsychological profile germane to HIV infection in the brain, potential confounding factors relating to the systemic involvement of the disease should be controlled for. For this purpose, it was initially proposed that a second patient population, one

analogous to the AIDS sample with respect to the severity and progressive nature of the illness, multiple therapeutic management, recurrent lapses, and poor prognosis, be chosen as a comparison group. Multiple attempts were made to obtain the cooperation of cancer and/or leukaemic patients, however my endeavours toward this end were unsuccessful.

Another important aspect that pertains to the description of the neuropsychological profile or to the clinical manifestations of a particular syndrome is the issue of differential diagnosis. Similarities and differences associated with the presenting features of a specific syndrome are contrasted with that of other related-disease syndromes. The ARC patient population shares many characteristics of the full blown AIDS, and given the close association between the two syndromes, it has been investigated as well.

Design of the Study

This study depicts the neuropsychological and psychological features characterized by 2 medically-defined groups, the AIDS and the ARC patients; and two control comparison groups of healthy homosexual men, one testing positive and one testing negative to HIV exposure.

The specific hypotheses for the neuropsychological test battery are:

HYPOTHESIS 1: Nonhealthy participants will achieve scores indicative of lower performance than members of the healthy groups. In view of the absence of HIV-related symptomatology, the latter groups (HIV- & HIV+) are expected to display comparable levels of performance.

HYPOTHESIS 2: The AIDS group will display a poorer neuropsychological profile than that of the ARC, HIV+, and HIV- groups.

HYPOTHESIS 3: Univariate differences are predicted between the ARC and the healthy groups (HIV- & HIV+) on the most taxing tests only, such as the Consonant Trigrams and the PASAT. Overall group differences are not expected between the ARC and the AIDS group in view of an overlap of impaired performance.

The specific hypotheses for the personality/emotional tests are:

HYPOTHESIS 4: Nonhealthy groups will display more emotional dysfunction on all three measures of psychological functioning (MMPI, SIP, and STAI) than the healthy ones. No differences between the two healthy groups are expected.

HYPOTHESIS 5: The AIDS group will display greater profile elevation on the MMPI, and report more behavioural dysfunction related to illness on the SIP than the remaining three groups.

HYPOTHESIS 6: The ARC group will disclose greater anxiety levels than the AIDS group.

HYPOTHESIS 7: In comparison to the healthy groups, ARC patients will exhibit a greater pattern of emotional dysfunction overall (i.e. on the MMPI, SIP, and STAI).

CHAPTER FOUR

RECENT DEVELOPMENTS

AIDS definition

With the increasing identification of associated neurological complications as well as the occurrence of neurological manifestations as the initial symptoms of HIV infection, the CDC revised and expanded the initial surveillance definition of AIDS, and proposed a new classification system for the entire spectrum of HIV infection (see CDC, 1988). Four major groups were identified: Group I represents the primary acute infection which appears as a self-limited mononucleosis-like illness. Group II consists of an asymptomatic carrier state. Group III comprises the persistent generalized lymphadenopathy only, and Group IV encompasses all other diseases. Patients in the latter group are assigned to one or several subgroups on the basis of their clinical symptomatology, and this classification is made independently of the presence or absence of lymphadenopathy. Within each subgroup, patients may range from being minimally symptomatic to severely ill. The subgroups are:

Subgroup A: Constitutional Disease (previously known as AIDS-Related Complex or ARC)
Subgroup B: Neurologic Disease
Subgroup C: Secondary Infectious Diseases
Subgroup D: Secondary Cancers
Subgroup E: Other Conditions of HIV Infection (not classifiable in the above)

The primary neurologic disease may include one or more processes such as dementia (encephalopathy), vacuolar myelopathy, atypical aseptic meningitis, and/or peripheral neuropathy, and this in the absence of a simultaneous ailment or condition other than HIV infection to account for the presentation (CDC, 1988).

Some studies classify HIV+ individuals according to an alternative stratification system, the Walter-Reed Stages (WR0 to WR6) (Redfield, Wright, & Tramont, 1986).

HIV-2

AIDS has a worldwide distribution and has been associated with HIV infection in the United States, Western Europe, and Central Africa. However, many of the clinically diagnosed AIDS patients from Western Africa failed to demonstrate serological detection of HIV antibodies until a new human retrovirus was isolated and initially named LAV-2 (Clavel, Guetard, Brun-Vezinet, et al., 1986) or HTLV-IV (Kanki, Barin, M'Boup, et al., 1986). This second human retrovirus which also causes AIDS, now known as HIV-2, is prevalent primarily in West African countries and has reportedly been present in this population since 1966 (Kawamura, Yamazaki, Ishikawa, et al. 1989). By the end of 1988, most western European countries also reported HIV-2 infected persons, with a total of 338 cases (Hampl, 1989). Only a negligeable number of HIV-2 cases were detected in

the U.S. (Hampl, 1989), while Brazil appeared to have greater prevalence rates (Cortes, Detels, Aboulafia, et al., 1989; Veronese, Mazza, Santos-Ferreira & Lourenzo, 1987). However, reports published by the end of 1988 most likely underestimate the true prevalence of HIV-2 since the results were obtained from serological testing with HIV-1 screening assays which cross-reacted with HIV-2 antibodies. New assays to test for HIV-2 antibodies specifically, as well as combination test systems for HIV-1 and HIV-2 are available only since the beginning of 1989.

The mode of transmission and clinical presentation of HIV-2-related AIDS appear to be similar to HIV-1 (Hampl, 1989). Although HIV-1 and HIV-2 have morphological identities which cannot be differentiated by electron microscopy (Dawson, 1989), they are distinct retroviruses as they show some disparities in the base sequences of the nucleotides which contain their respective genomes, and in the amino acid sequences of their major structural proteins (Guyader, Emerman, Sonigo, et al., 1987). More striking similarities have been found between HIV-2 and SIV, a simian immunodeficiency virus which was initially isolated in macaques displaying an AIDS-like syndrome (Gyader et al., 1987).

There is some evidence to suggest that the incubation period leading to the full-blown syndrome is longer with HIV-2 than after exposure to HIV-1, and may extend over 10

years (Cortes et al., 1989; M'Boup, N'Doye, Ricard, et al., 1988; Veronese et al., 1987).

Pathogenesis

Preliminary investigations documented that HIV gains cell entry by attaching itself to the cell surface receptor site, the CD4 molecule, and that the T4-lymphocytes constituted the targeted cell population of the retrovirus. However, more recent studies have demonstrated that only a minute percentage of T cells are compromised (0.01%), and that macrophages and monocytes also express the CD4 cellular receptor, thus becoming possible host cells for HIV replication (Pert, Smith, Ruff, & Hill, 1988). Macrophages circulate among inflamed tissues thoughout the body, including the brain, and appear to be less susceptible to the cytopathic effects of HIV. They may thus serve as a persistent viral reservoir (Kornbluth, Oh, Munis, et al., 1989).

Neuropathology of HIV infection

Virological and morphological studies have irrevocably substantiated that HIV infiltrates the brain and can replicate itself. A predilection for specific cell types has been noted in the monocytes and macrophages lineage primarily (Koenig, Gendelman, Orenstein, et al., 1986; Popovic, Mellert, Erfle, & Gartner, 1988; Wiley, Shrier,

Nelson, et al., 1986), but also in endothelial cells (Wiley et al., 1986), glial cells such as oligodendrocytes and astrocytes (Cheng-Mayer, Rutka, Rosenblum, et al., 1987; Levy, Evans, Cheng-Mayer, et al., 1987), and microglia, pericytes, and neuronal cells (Popovic et al., 1988). HIV encephalitis produces pathological alterations primarily in the cerebral white matter initially, and implicates the subcortical grey structures and cerebral cortex with progression of the disease (Petito, 1988). Macroscopic examination reveals mild to moderate atrophy. At the microscopic level, 90% of HIV infected brains show diffuse myelin pallor of the centrum semiovale (de la Monte, Ho, Schooley, et al., 1987; Navia, Cho, Petito, & Price, 1986). Other documented findings include scattered gemistrocytic astrocytosis, mild infiltration by rod cells, lipid-laden macrophages, and lymphocytes (Petito, 1988). Parenchyma and tissue adjacent to small blood vessels suffer small foci of demyelination or small collections of mononuclear cells which are poorly circumscribed. White matter and glial nodules bear scattered multinucleated cells. The subacute encephalitis associated with these multinucleated cells is said to be histopathologically characteristic and distinctive of children and adults with AIDS (Petito, Cho, Lemann, et al., 1986). The number of multinucleated cells and multinucleated giant cells is directly correlated with the severity of the pathological changes, and the severity

of the AIDS dementia complex, especially when grey and white matter abnormalities involve the frontal and temporal lobes (de la Monte, et al., 1987). The subcortical structures, the caudate and putamen in particular, feature neuronal loss associated with reactive astrocytosis and rod cell infiltration. The more severely affected brains display grey and white matter abnormalities which are widely distributed throughout the CNS. Although the cerebral hemispheres are most prominently implicated, lesions have been observed in the cerebellum, the brainstem, and the spinal cord (Petito, 1988).

In contrast, benign histopathological changes have also been noted in 33% of cases presenting with severe neurological dysfunction (Navia, et al., 1986a). This observation has lead to the suggestion that indirect mechanisms may also be at play in the dementia process. Yarchoan and his collaborators (1988) proposed that HIV-infected cells may yield neurotoxic factors within or outside the CNS which would induce neurological dysfunction. Findings from early research have provided some support for this. For example, HIV-infected victims have shown increased serum levels of an acid-labile alpha-interferon (Eyster, Goedert, Poon & Preble, 1983), while treatment for Kaposi's sarcoma with interferon has resulted in confusion and other neurological signs (Groopman, Gottlieb, Goodman, et al., 1984). Administration of azidothymidine (AZT) in

AIDS patients has contributed to a marked decrease in their serum interferon levels over 2 to 6 weeks, suggesting that the reduction in interferon levels may underlie the improvement in cognitive functioning (Yarchoan, Thomas, Grafman, et al., 1988).

Treatment

Much research has been aimed at discovering an anti-retroviral agent that could inhibit the infectivity and cytopathic effect of HIV. To date, azidothymidine (AZT or 3'-Azido-2',3'-dideoxythymidine) represents the only medication approved by the Food and Drug Administration to remedy HIV infection. It has been reported to be an effective inhibitor of HIV infection in vitro (Mitsuya, Weinhold, Furman, et al., 1985), and shown promise in clinical trials (Fischl, Richman, Grieco, et al. 1987). Its mode of action is to terminate the chain synthesis of viral DNA. The efficacy of clinical drug trials is being investigated from different perspectives: improvements in immunological measurements, decreases in mortality and incidence of opportunistic infections, and changes in mental status. Although AZT treatment seems to prolong life, drug toxicity and progression of immunodeficiency nevertheless impede survival (Cox, Martin, Styer, & Beall, 1989; Miller, Peterson, Davidson & Cohn, 1989). Published longitudinal studies are still relatively short in duration

(approximately 2 years). For instance, a group of 60 ARC patients were treated with AZT over one year and all but one revealed no evidence of clinical disease progression (Cuneo-Crovari, Cassola, Crovari, et al. 1989). From immunological and virological perspectives however, the HIV infection was still progressing but at a slower rate than in untreated patients. Clinical observations are now starting to indicate a window of 18 to 24 months or so during which the drug is only effective at postponing the emergence of symptoms and reducing the cythopathic effect of HIV infection, and not at completely arresting the disease progression per se (Garber, 1989).

AZT is highly toxic from an haematological point of view; it can cause severe anemia, granulocytopenia, thrombocytopenia, headaches, mild confusion or anxiety, nausea, skin rashes and itching. Agitation, restlessness, and insomnia have also been observed with high doses. Consequently, treatment must often be interrupted, and the increase in body weight and CD4 cell counts may be transient (Dournon, E., Matheron, S., Rozenbaum, W., et al., 1988). One of the earlier study conducted by Kennedy and his collaborators (1987) suggested that patients treated with AZT showed improvement on the neurological examination but no observable neuropsychological changes were detected when compared to placebo treated individuals. However, the validity of these findings was questionned given the

composition of the study sample; the majority were neurologically normal and only a small number had mild neurological involvement (Price, Sidtis & Rosenblum, 1988). Subsequent studies revealed positive effects in the initial study period of AZT-treated patients when compared to placebo controls (e.g. Schmitt, Bigley, McKinnis, et al., 1988; Yarchoan, et al., 1988). More specifically, the performance of a series of neuropsychological screening measures was found to be notably better in the AZT-treated group than the untreated one, despite a lack of change in the overall neurological status (Sidtis, Sadler, Keilp, et al., 1989). A significant improvement was also found on CD4 cell count. However, findings remain equivocal and further investigations are warranted, as reports have also described variable long term benefits, with some patients showing an initial improvement in performance and subsequently deteriorating or dying despite the treatment (Reinvang, Lundervold, & Froland, 1989). The therapeutic agent apppears to have no psycho-stimulating effect on performance of individuals who function normally (Reinvang et al., 1989).

AIDS-dementia complex (ADC)

Recent reports detailing the incidence of AIDS-dementia complex as the first manifestation of AIDS range from 5.9% in a small Spanish (Barcelona) sample (n=102) (Abos, Graus,

Alom, et al., (1989), to 9% in an Italian (Rome) based sample (n=217) (Galgani, Piazza, Antonucci et al., 1989). In a much larger U.S. (San Francisco) sample (n=5834), the incidence was 7.1%, with escalations ranging from 1.9% of total cases in 1982 to 9.4% in 1988 (Wilson, Lemp, Neal, et al., 1989). This apparent increase reflects in part the change in the AIDS definition adopted in 1987. Examination of the epidemiological characteristics revealed that AIDS patients manifesting CNS involvement were more likely to be older, to belong to the heterosexual intra-venous drug user risk group, and to have a shorter survival period than people with neurological disease. No patterns were noted with respect to ethnicity/race or gender. In later stages of the disease, 28% of advanced ARC and AIDS patients under AZT treatment met the criteria for dementia over a period of two years (Day, Grant, Atkinson, et al., 1989). The occurrence of ADC is considered to be a poor prognostic sign despite improved neuropsychological function in response to AZT (Reinvang et al., 1989).

Emerging studies of altered brain function suggest that the ADC presents as a subcortical type of dementia, with patients displaying diverse constellation of cognitive, motor, and behavioural disorders (Price, et al., 1988). Impaired concentration abilities, difficulty in performing complex sequential mental activities, reduced problem solving skills, and deficient memory on tasks necessitating

flexibility and concentrated effort constitute the initial signs of cognitive dysfunction. Functional disabilities arise with problems in reading and in executing the more taxing mental efforts at work or in daily life situations. Discernable aphasia, amnesia, or parietal lobe syndromes only become apparent in the later stages of the disease. Early motor disturbances usually implicate the lower extremities more often than the upper limbs, and are characterized by clumsiness and altered gait. The upper extremities occasionally reveal changes in hand-writing or difficulties with fine movements. Apathy, aspontaneity, social isolation, and personality alterations constitute the most prominent behavioural observations. Less frequently seen are anxiety, hyperactivity, and inappropriate behaviour. Aronow and his collaborators observed that patients with mild cerebral atrophy may not necessarily reveal obvious neurological impairment, and that severe atrophic changes were correlated with progressive ADC and deterioration in neuropsychological functioning (Aronow, Keilp, Krol, et al., 1989).

The subcortical character of HIV-related dementia has also been confirmed by use of a discriminant analysis. The neuropsychological profiles of HIV infected patients were submitted to a classification rule which could effectively discriminate patients who are cognitively intact from those who demonstrate cortical (Alzheimer) or subcortical

(Huntington) forms of dementia (Brouwers, Mohr, Hendricks & Baron, 1989). The discrimination function classifed 65% of HIV+ patients as normal, and 35% as demented, with 83% of the demented patients displaying a subcortical profile and only 17% a cortical pattern (Brouwers, Mohr, Hendricks, et al., 1989).

Early implication of the basal ganglia or of the nigrostriatal system was postulated by Martin and his collaborators following the observation that HIV+ (symptomatic and asymptomatic) individuals were impaired in egocentric spatial ability (Money Road Map & Room Test) (Martin, Kampen, Salazar, et al., 1989). These conclusions were based on previous findings which indicated that Huntington and Parkinson patients were also deficient in the performance of these tasks (Martin, Robertson, & Edelstein, 1989c).

A number of other diagnostic techniques have contributed to associate subcortical structures with the ADC. For example, the topographic distribution of CNS microglial nodules and multinucleated giant celles was investigated in a sample of 30 patients presenting with HIV-related subacute encephalitis. The basal ganglia and brainstem displayed microglial nodules more frequently than other areas, while the pallidum and white matter primarily contained giant cells (Henin, Reux, Vazeux, et al., 1989). An analysis of regional glucose metabolism via positron

emission tomography (PET) or by use of fluorodeoxyglucose revealed metabolic changes implicating the subcortical regions and their connections with the cortex (Rottenberg, Moeller, Strother, et al., in press). It has been suggested that glucose hypermetabolism in the basal ganglia and thalamic regions may represent an early feature of the ADC, while global hypometabolism and disturbance of the subcortical-cortical connections gradually occur with disease progression. In another study, a reduction in cortical choline acetyltransferase activity compatible with alterations in subcortical pathways was noted in brains of patients with ADC (Navia, Kahn, Pumarola-Sune & Price, 1986). A similar finding in nondemented patients implied that subclinical alterations in enzymes and mild myelin pallor may arise in the initial phases of the infection.

Pigorini, Pau, Galgani, et al. (1989) used a single photon emission computed tomography (SPECT) to document brain involvement, and observed pathological findings such as cortical thinning, cortical focal hypoperfusion, as well as basal ganglia hypoperfusion in all of their sample cases. There appeared to be a predilection for frontal cortex in cortical hypoperfusion (64%). In view of these findings, Pigorini et al. (1989) suggested that the SPECT cerebral blood flow may be more sensitive than CT and MRI in identifying pathophysiological dysfunction in the early stages of the disease.

Neuropsychological studies

A number of recent studies aim at the early detection of HIV-related dementia. For this purpose, they have combined novel computerized methods of assessment in addition to traditional neuropsychological measures to facilitate the ascertainment of subtle abnormalities which prove to be elusive in the early stages. To investigate the presence of cognitive slowing in particular, duration of decision-making and central processing has been assessed via multiple-choice reaction time (RT) paradigms. Preliminary investigations have revealed interesting results.

Miller, Satz, and Visscher (1989) reported a decline in performance on computerized RT tests in 29% of HIV+ (N=224) and 18% of HIV- (N=246) individuals over the course of 6 months. These proportions were found to be statistically different from each other in the background of stable performance on the conventional neuropsychological screening battery. However, a third follow-up visit did not replicate the greater decline of HIV+ individuals on computerized tests (Miller, Satz, Van Gorp, et al., 1989).

Another study compared measures of decision-making speed for simple and choice RT, (Martin, Robertson, & Edelstein, 1989c & 1989d). Increased decision-making time was documented in both asymptomatic HIV+ and ARC patients. Only the latter group obtained mean time scores which proved

to be statistically longer than those of seronegative controls. These findings were observed in the absence of group differences for simple RT and a control task of encoding speed (Martin et al., 1989c & 1989d). In a different sample, choice RT measurements were also found useful in discriminating AIDS patients from seronegative controls, but were less sensitive for ARC and asymptomatic individuals (Perdices & Cooper, 1989).

Consistent with these findings, Martin and his co-workers reported that although HIV+ individuals achieve comparable levels of accuracy on procedural or skill learning tests (maze learning), their performance time is much slower (Martin, et al., 1989a). On the other hand, computerized memory tests were considered less sensitive than traditional neuropsychological measures in differentiating a) HIV asymptomatic individuals from ARC patients, b) neurologically normal from neurologically abnormal individuals, and c) patients with normal T4 cell counts from those with abnormal levels (Syndulko, Singer, Ruane, et al., 1989).

Based on their findings, Martin et al. (1989c) have argued that standard clinical neuropsychologic tests have not yielded reliable indices of cognitive abnormalities in published studies and suggested that RT-based prodedures be used as they may prove to be more discriminatory and consistent. However, the differentiation of seropositive

and seronegative groups may be markedly increased by the use of both types of measures. When RT tests were taken in combination with conventional neuropsychologic measures, they were found to be more successful in discriminating asymptomatic and ARC patients from controls (Miller et al, 1989a; Percides & Cooper, 1989).

Investigations which have used the administration of comprehensive neuropsychological test batteries have also produced discrepant findings. Baseline and longitudinal data from the Multicenter AIDS Cohort Studies (MACS) did not reveal greater incidence of neuropsychological impairment or decline between asymptomatic HIV-infected individuals and noninfected controls (Selnes, McArthur, Miller, et al., 1989; Selnes, Miller, McArthur, 1989). Similarly, Tross and her colleagues (1988) noted significant impairment in motor speed, fine motor control, concentration and visuospatial problem solving in two AIDS patient groups: one recently diagnosed with full-blown AIDS and AIDS patients referred for neurological consultation, while HIV antibody negative and HIV antibody positive groups remained stable. Neuropsychological profiles of asymptomatic HIV+ individuals bearing CD4 cells less than 400 were comparable to those with CD4 cells greater than 400 (Dilley, Boccellari, Davis, et al., 1989). Additionally, this pattern was also held constant when comparing HIV+ individuals with CD4 less than 400 and seronegative controls. Belsky-Barr, Perry, Swanda,

et al. (1989) reported no significant differences between asymptomatic HIV+ individuals and seronegative controls when using conservative statistical methods to analyse the neuropsychological performance scores. However, exploratory analyses disclosed greater variability among HIV+ than HIV- patients which they interpreted as an index of mild impairment in functioning.

Several research teams have reported conflicting findings to the aforementioned studies in reporting evidence of compromised neuropsychological functions. Alterations in cognition were observed not only in ARC and AIDS patients but have also been reported in medically asymptomatic individuals and early in the course of HIV infection (Claypoole, White, Townes, et al., 1989; Clifford, Miller, Seyfried, et al., 1989; Collier, Marra, Coomgs, et al., 1989; Grant, Atkinson, Hesselink, et al., 1987 & 1988; Krikorian, Wrobel, Meinecke, et al., 1989; Stern, Sano, Goldstein, et al., 1989a). In one particular instance, neuropsychological deficits were reported in approximately 50% of patients presenting with LAS syndrome (CDC stage III) as the only symptoms (Janssen, Saykin, Kaplan, et al., 1988).

Comparison of neuropsychological functions between ARC and AIDS patients have also produced disparate results. Focusing on long-term storage and on consistent longterm retrieval aspects of memory functions, Fernandez, Levy, and

Pirozzolo (1989) reported significant abnormalities in both groups as evidenced by the following proportions: 62% of ARC and 73% of AIDS patients achieved scores exceeding one standard deviation below the mean on long-term storage, while 92% of ARC and 100% of AIDS cases fell one standard deviation below the mean on consistent long-term retrieval. They also observed disturbances in visual scanning, information processing, and attention abilities. In contrast, Van Gorp and his colleagues noted that performance of AIDS patients, on a comprehensive battery of neuropsychological tests, was markedly poorer than both ARC and HIV- groups on several measures (Van Gorp, Miller, Satz, & Visscher, 1989a & 1989b). These incorporated timed and untimed measures of visual constructional skills, tests of motor speed and cognitive flexibility, as well as several indices of nonverbal memory. In the background of these findings, the groups failed to differ on any measures of attention, language, verbal memory, or Mini-Mental State Examination (MMSE) scores.

The heterogeneity of findings with respect to neuropsychological abnormalities may stem from different methods and approaches to data analysis, use of dissimilar psychometric instruments, and sampling procedures. Several research groups have emphasized the need to include appropriately matched seronegative comparison individuals which belong to the population at risk (e.g. Belsky-Barr et

al., 1989; Marder, Bell, Dooneief, et al., 1989). For example, research conducted with the intravenous drug abusers (IVDA) has yielded more consistent results in identifying compromised higher mental functions. Neuropsychological disturbances are common in both HIV- and HIV+ IVDA and often noted in concentration, memory, mood, speed, and comprehension (step commands) (Royal, Cornblath, Updike, et al., 1989; Selnes, Proctor, Royal, et al., 1989). These results underscore the importance of homogeneous samples with respect to risk behaviours. Substance abuse and nutritional factors have confounding effects which need to be teased out from HIV infection in order to determine the etiology of neurological involvement adequately. The studies which have reported neurological implications in mildly symptomatic HIV+ individuals have often obtained such findings in an heterogeneous sample, i.e. one including IVDA (e.g. Chave, Thuillard, Assal, & Glauser, 1989).

Furthermore, some investigations contrasted HIV- and HIV+ samples which were not always commensurate in attribute variables such as age, education, and lifestyle characteristics (e.g. Clifford et al., 1989; Collier et al., 1989). The inclusion/exclusion criteria for the HIV+ group are not always explicit and identical; while some studies combine ARC patients with mildly symptomatic and asymptomatic individuals within their HIV+ sample, other investigations will be more restrictive and form several

HIV+ subgroups thereby delineating the various spectrum of the disease.

More recently, studies have also investigated the contribution of psychological factors such as reactive depression and anxiety which occur in association with HIV infection as these may affect the cognitive performance of HIV infected patients. Most of them concur that the cognitive decline observed in HIV victims cannot be attributed solely to mood disturbance and attentional changes (Kovner, Perecman, & Lazar, 1989). Interestingly, the degree of self-reported cognitive deficits was not found to be consistently related to an objective assessment of cognitive performance (Herns, Newman, McAllister, et al., 1989). Instead, it was associated with elevated scores on mood state measures (both self-report and observer-rated).

Thus, much of the more contemporary research findings advocate the relevance of the current reseach proposal. Had the breath of knowledge summarized in this chapter been available at the time of the proposed investigation, minor modifications would have been incorporated in the choice of the neuropsychological test battery. However, the design of the study would have essentially remained the same. These changes will be highlighted in the general discussion following the interpretation of the results.

CHAPTER FIVE

METHODOLOGY

Subjects

Fifty-nine male homosexuals agreed to participate in a study investigating the psychological and neuropsychological characteristics associated with the acquired immune deficiency syndrome. Control/comparison group volunteers were matched for age, education and socioeconomic status to the AIDS patient sample. Participants were all residents of British Columbia: 86% from the Greater Vancouver area, 12% from Victoria, and 2% from the B.C. interior (Kelowna).

Volunteers were recruited from several sources in order to assure sufficient sample size. The author presented short talks discussing the objectives of the study, and provided posters describing these to health care practitioners, community agencies/organizations, and support groups servicing the population at risk. Table 5.1 summarizes the distribution of the various sources who provided their cooperation and from which respondents were obtained. Participants were screened for previous history of psychiatric disorder, neurological disease, severe longstanding substance abuse, and incidents of head injury causing unconsciousness. Those who did not have recent and/or previous HIV screening test underwent laboratory testing for the presence of HIV antibodies in the blood.

Table 5.1

Source and Distribution of Participants

Health care practitioners		**46%**
Individual members of the multidisciplinary AIDS Care Committee at St-Paul's Hospital (Vancouver)	37%	
Other physicians of the Greater Vancouver area	9%	
Community agencies/organizations		**27%**
Gay & Lesbian Organization of the University of Victoria	12%	
Newspaper Advertisement	9%	
AIDS Vancouver	3%	
Vancouver Persons with AIDS (PWA) Coalition	3%	
Support groups		**13%**
Family, Partners, & Friends Support Group (Vancouver)	10%	
Testing Positive Drop-in & Support Group (Vancouver)	3%	
Word of mouth		**14%**

The 59 volunteers were divided into four groups according to their health status and the serological findings. The groups were sampled as follows:

1) healthy individuals, seronegative for HIV (HIV-, n=17);
2) healthy individuals, seropositive for HIV (HIV+, n=14);
3) symptomatic and/or ARC patients (ARC, n=14);
4) full-blown AIDS patients (AIDS, n=14).

Group assignment of each individual was confirmed with the family physician. Selection criteria for the AIDS patient group included a recent diagnosis of AIDS (within 3-6 months), and no evidence of neurological symptoms present. Inclusion in the ARC patient group was determined by method of exclusion, i.e. nonhealthy and non-AIDS, also free of neurological involvement. Table 5.2 lists the mean age and years of education for each group.

Table 5.2

Demographic Information for Each Group: Mean Age and Mean Years of Education (SD)

Subject Group		n	Age	Education
Healthy:	HIV-	17	33.8 (10.1)	13.4 (2.3)
	HIV+	14	33.6 (6.3)	13.6 (2.0)
Nonhealthy:	ARC	14	30.9 (6.4)	12.7 (2.2)
	AIDS	14	35.7 (7.8)	12.8 (2.0)

Material

A wide range of tests was chosen to assess the neuropsychological/cognitive functions, including the motor and sensory abilities. The objective was to obtain measures of screening for signs of cerebral dysfunction. The personality and functional status of the participants were also examined.

The Wechsler Adult Intelligence Scale-Revised, (WAIS-R, Wechsler, 1981), was administered to obtain a measure of verbal and nonverbal intellectual abilities. Other cognitive functions investigated included mental tracking abilities and rapidity of information processing using the Paced Auditory Serial Addition Test, PASAT (Gronwall & Sampson, 1974; Gronwall & Wrightson, 1974). The Trail Making Test (Army Individual Test Battery, 1944) provided a screen for divided attention and mental flexibility.

Immediate and delayed recall of verbal memory was evaluated with the short passages of Form 1 of the Wechsler Memory Scale (Stone, Girdner, & Albrecht, 1946; Wechsler, 1945), and the word lists of the Rey Auditory Verbal Learning Test (Rey, 1941; Taylor, 1959). Analogous visual items were used to rate short and longterm nonverbal memory abilities: the Rey-Osterrieth Figure (Osterrieth, 1944; Rey, 1941), and the Rey Nonverbal Learning Test (Rey, 1964). Memory in the face of interference was examined using the

Brown-Peterson technique, (Brown-Peterson Consonant Trigrams Auditory Memory Task - CCC, Brown, 1958; Peterson & Peterson, 1959; Peterson, 1966).

Assessment of visual perception included examination of visual scanning abilities, (Visual Search Test, Goldstein & Shelly, 1973), visual recognition, (Test of Facial Recognition, Benton & Van Allen, 1968; Benton, Hamsher, Varney, & Spreen, 1983), and conceptual organization, (Hooper Visual Organization Test, Hooper, 1958). Of the language skills, naming, (Boston Naming Test, Kaplan, Goodglass, & Weintraub, 1978), comprehension, (Short Form Token Test, (Spellacy & Spreen, 1969), and verbal fluency, (Controlled Oral Word Association Test - FAS, Spreen & Benton, 1977) measures were administered.

Tactile recognition and discrimination skills were examined by the Finger Localization Test (Benton, 1959; Benton et al., 1983), and the Tactile Form Perception Test (Benton et al., 1983). Right-left discrimination of body awareness was also examined with the Right-Left Orientation test (Benton et al., 1983). Assessment of motor functions involved measures of fine motor movement (Finger Tapping Test, Reitan & Davison, 1974; Russell, Neuringer, & Goldstein, 1970), and hand grip strength (Dynamometer, (Reitan & Davison, 1974).

The psychological assessment consisted of an objective test of personality (MMPI, Colligan, Osborne, Swenson &

Offord, 1983; Hathaway & McKinley, 1951; Welsh & Dahlstrom, 1956; Dahlstrom, Welsh, & Dahlstrom, 1975), a self-rating scale of anxiety, (State Trait Anxiety Inventory, Spielberger, Gorsuch, & Lushene, 1970), and one of health related behavioral dysfunction, (Sickness Impact Profile, Bergner, Bobbitt, Pollard, Martin & Gilson, 1976).

Procedure

Each participant read a statement of intent (Appendix A) and signed a standard consent form (Appendix B). Upon request, each participant also received the opportunity to have a summary of their test results forwarded to their family and/or referring physician.

A personal identification number was assigned to each volunteer. All personal identifying information was removed from a person's file and all material was labelled with the personalized ID number. The consent forms were kept in a separate folder. This identification number consisted of a letter code for group assignment (i.e. A= HIV-, B=HIV+, C=ARC, and D= AIDS), and a subject number within that group (1 to 17). The participants were blind as to the letter code although the majority knew which group they belonged to. This precaution was taken however, because a few participants preferred to remain unaware of the serological results from their HIV screening test.

Each participant received a card with the following information: 1) title of the study; 2) name of the investigator; 3) institutional affiliation of the investigator; 4) personalized ID number; 5) date of assessment; and 6) whether or not the participant requested that the results be transmitted to his physician. With this card, any participant who had originally declined this option, could, at any later date, request that the test results be forwarded to a health care practitioner of his choice.

Participants were assessed individually and on the basis of availability. Rest periods were determined at the examinee's discretion, and testing sessions could be broken up into 2 or 3 consecutive days. The order of test administration (see Table 5.3) was generally kept constant, being flexible for the number of interleaving test between immediate and delayed memory recall measures, and making allowances for the need to rest, and/or resume a testing session. It was deemed preferable to perform a brief semi-structured personal interview towards the end of the assessment. At this point, the investigator would have had ample time to develop a good rapport with the participants. Topics covered included a description of their health status (present and past symptomatology), medication regime, frequency and nature of substance abuse, previous history of traumatic brain injury involving loss of consciousness,

Table 5.3

General Order of Test Administration

First Session

Statement of Intent
Consent Form

Lateral Dominance Examination
Wechsler Adult Intelligence Scale-Revised (WAIS-R)
Information
Wechsler Memory Scale (WMS) Logical Memory
WAIS-R Picture Completion to Vocabulary
WMS Logical Memory 30-minute Recall*
WAIS-R (continued to end)
Petersen Consonant Trigrams
Right-Left Orientation Test
Finger Localization
Tactile Form Perception
Finger Tapping
Dynamometer
State-Trait Anxiety Inventory
Sickness Impact Profile

Second Session

Paced Auditory Serial Addition Test
Rey-Osterrieth Copy
Controlled Oral Word Association Test (FAS)
Rey-Osterrieth 3-minute Recall
Rey Auditory Verbal Learning Test
Rey Nonverbal Learning Test
Hooper Visual Organization Test
Trail Making Test
Test of Facial Recognition
Boston Naming Test
Short Token Test
Rey Auditory Verbal Learning Test 30-minute Recall*
Visual Search Test
Rey Nonverbal Learning Test 30-minute Recall*
Semi-structured Interview
Minnesota Multiphasic Personality Inventory

* Approximate order taking into account a minimum of 30 minutes for delayed recall

previous history of psychological and/or psychiatric interventions, and a statement regarding their sexual activities (safe sex and/or promiscuity).

After the completion of the assessement, another appointment was scheduled for each volunteer to provide feedback regarding their performance on the test battery and answer any questions they may have had. The data collection extended from March 1986 to September 1987.

CHAPTER SIX

RESULTS

Synopsis

This chapter discusses the results of the primary and exploratory statistical analyses conducted in this study. Neuropsychology has only recently contributed to the investigation of HIV and its effect on the brain. Thus, in addition to testing the specific hypotheses, various aspects of the data have been explored to provide applicable information for future research in this area. The findings are summarized as follows:

1) Epidemiological characteristics:

   i) Descriptive statistics of demographic variables such as personal information, medical history, and life-style related data (interview) were compiled for the entire subject sample and individual group designations.

   ii) Group comparisons, using nonparametric statistics, were carried out according to health status and medical diagnosis. The nonparametric analyses substantiated the homogeneity of the groups with respect to personal information, medical history, and life-style.

2) Results of the neuropsychological assessment:

   i) Descriptive statistics are reported for the total sample of volunteers, as well as for each group denomination. A principal component analysis (PCA) was

performed on the neuropsychological data bank in order to abridge the test battery. This allows the identification of the underlying dimensions that may then be used to devise a method of assessment that is less time consuming.

ii) Group comparisons stemming from the stated hypotheses were conducted according to the subject's health status and medical diagnosis. This exploratory investigation included a wide selection of measures resulting in a less than optimal subject-to-variable ratio. In an attempt to control for this, group differences were tested from two perspectives: mean raw scores and mean factor scores. These statistical manipulations address the primary aim of this investigation, which is to verify the existence of a chronic subclinical AIDS encephalopathy in HIV infected individuals.

3) Psychological and Emotional aspects:

i) Descriptive statistics are summarized for the total sample and for each group denomination.

ii) Contributory underlying dimensions of the MMPI and the SIP were determined by way of PCAs.

iii) Group comparisons according to health status and medical diagnosis were performed to evaluate psychological adjustment, mood, anxiety, as well as physical and psychosocial disabilities.

4) Relationship between the neuropsychological and the psychological data sets:

A canonical correlation was executed to determine the interdependence of the neuropsychological test performance and the psychological adjustment profiles.

Epidemiological Characteristics

This section provides a description of the total sample of homosexual men who agreed to participate in the study, and satisfied the inclusion/exclusion criteria (n=59). These data are presented in order to characterize the population at risk within the Vancouver/Victoria Areas, and to determine whether this sample pool exemplifies the population reported in published research and clinical studies. For this purpose, descriptive statistics are presented in the form of frequency analyses on the following variables: age, education, occupation, substance abuse, prescribed medication, and medical history. Group comparisons were conducted using nonparametric statistics (Chi Squares). Group differences were examined for health status (Healthy & Nonhealthy) and according to the medical diagnosis (Asymptomatic HIV- Asymptomatic HIV+, ARC, and AIDS). In order to compare group differences according to the health status of the participants, HIV- and HIV+ groups were collapsed together to form the Healthy group, while the ARC and the AIDS constituted the Nonhealthy group.

Total Sample

Participants ranged between 18 and 50 years of age, with the highest frequency (28.9%) falling between 31 and 35 years (Table 6.1). Grade 13 constituted the median level of education of the subject pool (Table 6.2). Percentages of volunteers who had not completed high school (<13 = 44.1%), and of those who attended college and/or university (>13 = 45.8%) were equivalent. Occupational data indicate that 55.9% were gainfully employed, while 40.7% were unemployed, and 3.4% were students with part-time work (Table 6.3). The majority (95%) of the sample was right handed (Table 6.4).

Only 5.1% of the total sample had never used any recreational drugs (Table 6.5). Of the remaining group, 78% had made regular or intermittent use of one or several drug types at some point in their life, while 22% had sampled experimental trials only. At the time of assessment, 62.7% were no longer making use of drugs. Table 6.6 lists the various types of illicit drugs ingested by the total sample.

With respect to alcohol consumption, (Table 6.7), 11.9% of the participants had never consumed alcohol. Of the 88.1% who described themselves as social drinkers, 28.8% felt that they had abused alcohol at one time or another in their life. At the time of this study, 22% of the total sample reported no intake of alcohol for medical reasons.

Table 6.1

Frequency Analysis of Age

(N = 59)

Age (years)	**Absolute Frequency**	**Relative Frequency (%)**	**Cumulative Frequency (%)**
< 20	1	1.7	1.7
21 - 25	9	15.3	17.0
26 - 30	10	16.9	33.9
31 - 35	17	28.8	62.7
36 - 40	9	15.3	78.0
41 - 45	7	11.9	89.8
46 - 50	6	10.2	100.0

Table 6.2

Frequency Analysis of Education

(N = 59)

	Absolute Frequency	**Relative Frequency (%)**	**Cumulative Frequency (%)**
High School			
Grade 8	2	3.4	3.4
Grade 9	1	1.7	5.1
Grade 10	4	6.8	11.9
Grade 11	4	6.8	18.6
Grade 12	15	25.4	44.1
Grade 13	6	10.2	54.2
College or University			
1 year	7	11.9	66.1
2 years	16	27.1	93.2
3 years	1	1.7	94.9
4 years	3	5.1	100.0

Table 6.3

Frequency Analysis of Occupation

(N = 59)

Status	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Employed	33	55.9	55.9
Unemployed	24	40.7	96.6
Student/ Part-time work	2	3.4	100.0

Table 6.4

Frequency Analysis of Handedness

(N = 59)

Handedness	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Right	56	94.9	94.9
Left	3	5.1	100.0

Table 6.5

Frequency Analysis of Recreational Drug Use

(N = 59)

	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Ingestion of Drug			
Yes	56	94.9	94.9
No	3	5.1	100.0
Frequency of Intake			
Experimental	13	22.0	22.0
Regular/sporadic	46	78.0	100.0
Use at Assessment			
Yes	22	37.3	37.3
No	37	62.7	100.0

Table 6.6

Frequency Analysis of Recreational Drug Type

(N = 59)

Drug Type	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Hallucinogens			
Yes	40	67.8	32.2
No	19	32.2	100.0
Narcotics			
Yes	8	13.6	13.6
No	51	86.4	100.0
Stimulants			
Yes	31	52.5	52.5
No	28	47.5	100.0
Depressants			
Yes	6	10.2	10.2
No	53	89.8	100.0
Cannabis			
Yes	56	94.9	94.9
No	3	5.1	100.0
Inhalant Nitrates			
Yes	29	49.2	49.2
No	30	50.8	100.0

Table 6.7

Frequency Analysis of Alcohol Use

(N = 59)

	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Social Ingestion			
Yes	52	88.1	88.1
No	7	11.9	100.0
Alcohol Abuse			
Yes	15	25.4	25.4
No	44	74.6	100.0
Use at Assessment			
Yes	46	78.0	78.0
No	13	22.0	100.0

While reviewing the medical history, 23.7% reported miscellaneous physical symptoms or medical conditions not related to HIV infection, and 20.3% complained of signs related to the CNS, i.e. headaches (Table 6.8). Clinical features germane to HIV infection were observed in 47.5%. Fourty-four percent reported sexually transmitted diseases. Almost half of the sample (44.1%) required therapeutic management for CNS-related complaints, while 35.6% were ingesting drugs treating HIV-related symptoms (Table 6.9). Medication for autonomic and cardiovascular problems were prescribed in 18.7%, and 1.7% received treatment for an endocrine disorder. Throughout their lifespan, 62.7% of the participants had consulted professionals such as psychiatrists, psychologists, and/or counsellors for supportive intervention (Table 6.10).

Group Differences

Group comparisons were conducted according to the participant's health status and medical diagnosis. One-way analyses of variance (ANOVA) produced F ratios which were not significant for age [$F(1, 58) = 0.904$, $p = .445$], and education [$F(1, 58) = 0.023$, $p = .880$]. The Healthy group averaged 33.7 years of age ($SD = 8.5$) and 13.5 years of education ($SD = 2.1$). The Nonhealthy group was 33.4 years old ($SD = 7.4$) and had achieved 12.8 years of education ($SD = 2.1$).

Table 6.8

Frequency Analysis of Medical Symptoms

(N = 59)

	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Non-HIV Symptoms			
Present	14	23.7	23.7
Absent	45	76.3	100.0
HIV Symptoms			
Present	28	47.5	47.5
Absent	31	52.5	100.0
CNS-related Symptoms			
Present	12	20.3	20.3
Absent	47	79.7	100.0
Sexually Transmitted Diseases			
Present	26	44.1	44.1
Absent	33	55.9	100.0

Table 5.9

Frequency Analysis of Prescribed Medication

(N = 59)

	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
HIV			
Yes	21	35.6	35.6
No	38	64.4	100.0
CNS			
Yes	26	44.1	44.1
No	33	55.9	100.0
Endocrine			
Yes	1	1.7	1.7
No	58	98.3	100.0
Autonomic/Cardiovascular			
Yes	11	18.6	18.6
No	48	81.4	100.0

Table 6.10

Frequency Analysis of Mental Health Interventions

(N = 59)

	Absolute Frequency	Relative Frequency (%)	Cumulative Frequency (%)
Use of Services			
Yes	37	62.7	62.7
No	22	37.3	100.0

Nonparametric statistics were used to analyse the medical history, personal, and lifestyle data. Results of the Chi Square analyses executed on the basis of health status revealed significant differences with respect to three variables only: occupational status, use of alcohol at the time of assessment, and presence of CNS-related symptoms (Table 6.11). The cell frequency distributions suggest that, at the time of evaluation, more nonhealthy individuals tend to be unemployed (68 vs 16%), more had stopped consuming alcohol (39 vs 6%), and more complained of headaches (36 vs 6%).

Age and education were equivalent for all four medical patient groups [$F(3, 58) = 0.904$, $p = .445$, and $F(3, 58) = 0.610$, $p = .612$, respectively]. Mean ages ranged from 30.9 for ARC ($SD = 6.4$), 33.6 for HIV+ ($SD = 6.3$), 33.8 for HIV- ($SD = 10.1$) to 35.9 for AIDS ($SD = 7.8$). Mean years of education attained varied from 12.8 for AIDS ($SD = 2.0$), 12.7 for ARC ($SD = 2.2$), 13.4 for HIV- ($SD = 2.3$), and 13.6 for HIV+ ($SD = 2.0$).

Frequency distribution analyses comparing the four medical diagnostic categories indicated that patient groups were homogeneous with respect to age, handedness, level of education, having ever ingested recreational drugs, having discontinued use of drugs at the time of assessment, types of recreational drug used (narcotics, stimulants, depressants, cannabis, and inhalent nitrates), social

Table 6.11

Group Comparisons of Epidemilogical Data for Groups Divided by Health Status (Healthy & Nonhealthy).

(N = 59)

Variables	Chi Squares	Degrees of Freedom	p values
Age	0.47	1	n.s.
Education	3.01	1	n.s.
Occupation	17.10	2	0.001
Ingestion of recreational drugs	1.20	1	n.s.
Pattern of drug intake	1.10	1	n.s.
Use of drugs at assessment	0.26	1	n.s.
Types of drugs			
Hallucinogens	3.85	1	n.s.
Narcotics	1.68	1	n.s.
Stimulants	2.12	1	n.s.
Depressants	0.09	1	n.s.
Cannabis	1.20	1	n.s.
Inhalant Nitrates	2.04	1	n.s.
Alcohol intake			
Social ingestion	0.90	1	n.s.
Temporary abuse	0.001	1	n.s.
Use at assessment	7.42	1	0.01
Medical Symptoms			
Non-HIV symptoms	0.49	1	n.s.
CNS-related signs	6.07	1	0.02
Sexually transmited diseases	2.76	1	n.s.
Type of medications			
CNS	2.76	1	n.s.
Autonomic/ cardiovascular	0.23	1	n.s.
Mental health intervention	0.26	1	n.s.

consumption of alcohol, history of sexually transmitted diseases, prescribed medication (CNS and autonomic/cardiovascular), and history of mental health interventions (Table 6.12). Significant differences were noted however on the following variables: occupational status, pattern of recreational drug intake, use of hallucinogens, reports of temporary alcohol abuse, alcohol ingestion at the time of assessment, presence of non-HIV symptoms, and reports of CNS-related signs, i.e. headaches (Table 6.12). Inspection of the cell frequencies suggest that a greater percentage of the ARC (50%) and AIDS (86%) patients were unemployed at the time of the evaluation (HIV- = 12%, HIV+ = 21%). Half (47%) of the HIV- group had used recreational drugs on an experimental basis, while the majority of the three remaining groups followed a more regular or sporadic pattern of ingestion (HIV+ = 93%, ARC & AIDS = 86%). Accordingly, fewer healthy sero-negative participants (35%) have sampled hallucinogens in contrast to the three HIV-infected groups (ARC = 86%, HIV+ & AIDS = 79%). Only one AIDS patient (7%) acknowledged abuse of alcohol at one point in time, while reports from other comparison groups ranged from 21% in HIV+ to 43% in ARC, (HIV- = 29%). More AIDS (43%) and ARC (36%) patients had stopped drinking alcohol prior to the time of assessment, either in view of their medical condition, or by personal choice (HIV- = 0%, HIV+ = 14%). In contrast to the other

Table 6.12

Group Comparisons of Epidemilogical Data for Groups Divided by Medical Diagnosis (HIV-, HIV+, ARC, & AIDS).

(N = 59)

Variables	Chi Squares	Degrees of Freedom	p values
Age	4.52	3	n.s.
Education	4.97	3	n.s.
Occupation	21.40	6	0.01
Ingestion of recreational drugs	7.38	3	n.s.
Pattern of drug intake	9.21	3	0.05
Use of drugs at assessment	3.28	3	n.s.
Types of drugs			
Hallucinogens	11.66	3	0.01
Narcotics	4.14	3	n.s.
Stimulants	7.41	3	n.s.
Depressants	4.33	3	n.s.
Cannabis	7.38	3	n.s.
Inhalant Nitrates	5.47	3	n.s.
Alcohol intake			
Social ingestion	4.77	3	n.s.
Temporary abuse	8.13	3	0.05
Use at assessment	10.20	3	0.02
Medical Symptoms			
Non-HIV symptoms	8.26	3	0.05
CNS-related signs	8.91	3	0.05
Sexually transmited diseases	4.82	3	n.s
Type of medications			
CNS	5.39	3	n.s.
Autonomic/ cardiovascular	4.43	3	n.s.
Mental health intervention	6.60	3	n.s.

three groups, none of the AIDS patients complained of, or had a medical history of non-HIV related symptoms (HIV- = 21%, HIV+ = 43%, ARC = 36%). However, more AIDS (29%) and ARC (43%) patients reported CNS-related signs, i.e. headaches (HIV- = 5%, HIV+ = 7%).

Frequency distributions of personal information, medical history, and life-style data described above are summarized in Appendices B-1 to B-10 for group assignment according to health status, and in Appendices C-1 to C-10 for medical diagnostic groups. AIDS was diagnosed on the basis of PCP in 64.3%, KS in 21.4%, and systemic lymphomas in 14.3%. Two (14.3%) PCP patients subsequently developed KS before they were seen for this study.

Neuropsychological Data

The primary objective of this study was to document the neuropsychological dysfunction associated with HIV infection. This section presents the results of the neuropsychological test battery. Group comparisons were conducted in order to verify specific a priori hypotheses. Additional analyses explored the relevance of particular functional areas in AIDS patients and related syndromes.

Total Sample

Table 6.13 contains measures of central tendency and dispersion scores of the neuropsychological data for the

Table 6.13

Neuropsychological Profile of the Total Sample

(N = 59)

Test	Mean	SD	Minimum	Maximum
Cognitive				
Full Scale IQ	110.98	11.63	84.00	136.00
Verbal IQ	110.85	11.52	88.00	134.00
Performance IQ	108.24	11.53	73.00	135.00
Attention/Concentration				
PASAT 2.4"	40.88	10.06	22.00	60.00
2.0"	36.64	10.65	17.00	60.00
1.6"	31.73	9.07	17.00	56.00
1.2"	24.03	7.07	10.00	48.00
Total Time*	13.93	3.68	7.60	25.10
Trail Making A*	28.59	9.72	13.00	61.00
Trail Making B*	67.25	31.75	26.00	240.00
Memory/Learning				
WMS Stories Immediate	13.00	2.98	6.75	19.00
Delayed	11.75	2.86	4.25	18.75
RAVLT Total 5 Trials	55.61	9.14	18.00	71.00
Delayed	12.10	3.13	0.00	15.00
Rey-Osterrieth Recall	21.59	5.69	4.50	33.00
RNVLT Total 5 Trials	42.25	11.49	19.00	62.00
Delayed	10.47	3.39	4.00	15.00
Consonant Trigrams	47.08	5.99	36.00	60.00
Visuospatial Perception				
Visual Search*	135.25	52.55	76.00	416.25
Facial Recognition	46.52	3.11	39.00	52.00
Hooper VOT	27.88	2.01	19.00	30.00
Rey-Osterrieth Copy	32.76	1.88	28.00	36.00
R-L Orientation	31.22	1.69	22.00	32.00

* Scores represent units of time

Table 6.13 (Continued)

Neuropsychological Profile of the Total Sample

(N = 59)

Test	Mean	SD	Minimum	Maximum
Language				
Word Fluency	45.75	11.72	21.00	82.00
Boston Naming	78.08	7.51	43.00	85.00
Token Test	77.34	1.01	73.00	78.00
Tactile Perception				
Tactile Form Pref.	9.64	0.76	7.00	10.00
Nonpref.	9.71	0.81	6.00	10.00
Time Pref.*	72.39	35.56	35.00	206.00
Time Nonpref.*	85.41	40.42	34.00	224.00
Finger Loc. Pref.	28.90	1.41	24.00	30.00
Nonp.	28.73	1.69	22.00	30.00
Motor				
Dynamometer Pref.	41.27	7.98	23.00	57.00
Nonpref.	37.41	7.12	21.25	55.50
Finger Tap. Pref.	58.23	6.34	41.00	71.00
Nonpref.	52.60	6.21	40.00	65.00
Lateral Preference	12.64	2.50	0.00	14.00

* Scores represent units of time

entire sample of volunteers. The listing includes means, standard deviations, and range (minimum, maximum) scores. WAIS-R subtests are tabulated in Appendix E-1. From a clinical point of view, mean scores all fluctuated within normal limits. High variability in level of performance was noted primarily for tests using time as a unit of measurement (e.g. Trail Making, Visual Search, Tactile Form Perception). Values of the remaining standard deviations were compatible with those from the published normative data available with each test, and suggest that the total sample was fairly homogeneous.

A PCA with varimax rotation was used to explore and redefine the neuropsychological data in terms of the underlying unique constructs. This analysis (Table 6.14) yielded six factor scores (eigenvalue > 1.0) which accounted for 70% of the variance. Meaningful factor loadings (> .7) are reported for each factor:

Factor 1: Trail Making Test (A + B), Visual Search, Tactile Form Perception (Time for dominant & nondominant hands).

Factor 2: Rey Nonverbal Learning Test and Rey-Osterrieth Complex Figure 30-delayed recall.

Factor 3: Boston Naming, Verbal IQ, and Dynamometer (dominant and nondominant hands).

Factor 4: Consonant Trigrams and Word Fluency.

Table 6.14

PCA of the Neuropsychological Data

(N = 59)

Final Statistics

Factor	Eigenvalue	Pct of Var	Cum Pct
1	7.49696	34.1	34.1
2	1.88921	8.6	42.7
3	1.88032	8.5	51.2
4	1.75541	8.0	59.2
5	1.28948	5.9	65.1
6	1.06132	4.8	69.9

Loadings of the Rotated Factor Matrix

	Factors					
Tests	1	2	3	4	5	6
Trails	-.834	-.271	-.110	-.214	.022	-.104
PASAT Total	-.693	-.090	-.046	-.438	.073	-.010
Stereognosis	-.743	-.385	-.042	-.003	.134	-.172
Visual Search	-.779	-.207	-.117	-.074	-.061	-.209
RNVLT Total	.253	.833	.104	.139	-.094	.030
Rey Recall	.327	.792	.107	.028	.058	.290
RAVLT Total	.543	.551	.215	.168	.037	-.194
WMS Stories	.128	.560	.404	.268	-.239	-.001
CCC Total	- 033	.373	.005	.754	.114	.004
F. Tapping Pref.	-.040	.069	.031	.048	.874	.133
F. Tapping Nonp.	.024	- 168	.001	.015	.852	-.155
Dynamometer Pref.	.351	.227	.656	-.180	.226	.158
Dynamometer Nonp.	.245	.311	.764	-.206	.100	-.028
Verbal IQ	.153	.084	.695	.468	-.096	.236
Word Fluency	.431	-.015	.185	.703	.033	.052
Boston Naming	-.069	.038	.812	.220	-.052	-.011
Token Test	.219	.264	.009	.376	-.132	.162
Performance IQ	.535	.150	.317	.266	.003	.464
Face Recognition	.170	.126	.084	.007	-.031	.836
Hooper VOT	.511	.225	.303	-.165	-.149	.258
R-L Orientation	.271	.020	-.041	.340	.216	.444
Finger Localization	.686	.068	.171	-.209	.169	.046

Factor 5: Finger Tapping (dominant & nondominant hands).

Factor 6: Facial Recognition Test.

For the total sample of participants, the common neuropsychological constructs underlying each factor can be interpreted as follows: 1) speed of information processing; 2) nonverbal memory; 3) verbal/language skills and grip strenth; 4) tasks tapping retrieval knowledge in the face of interference; 5) speed of fine motor movement; and 6) facial discrimination. The usefulness of the last two factors is somewhat limited as they are restricted to a single test each.

Group Differences

Table 6.15 lists the simple statistics of the neuropsychological test battery for groups defined by health status. Means and standard deviations of the WAIS-R subtests are reported in Appendix E-2. At first glance, the Healthy group seems to have achieved better mean scores than the Nonhealthy group on all measures, with the exception of Tactile Form Perception of the nondominant hand where the difference was expressed in decimal points. Difference in level of performance between these two groups was evaluated statistically using Wilk's criterion in a one-way multivariate analysis of variance (MANOVA).

Table 6.15

Neuropsychological Profile of Groups by Health Status

(N = 59)

Tests	Healthy (n = 31) Mean	SD	Nonhealthy (n = 28) Mean	SD
Cognitive				
Full Scale IQ	114.06	10.49	107.36	11.99
Verbal IQ	114.52	10.75	106.79	11.13
Performance IQ	110.35	11.09	105.89	11.75
Attention/Concentration				
PASAT 2.4"	42.87	10.15	38.68	9.66
2.0"	38.42	11.58	34.68	9.32
1.6"	34.23	10.12	28.96	6.90
1.2"	25.64	8.06	22.25	5.38
Total Time*	13.24	3.78	14.69	3.47
Trail A*	26.03	8.99	31.43	9.86
Trail B*	61.42	25.09	73.71	37.19
Memory				
WMS Stories Imm.	13.48	3.20	12.48	2.68
Del.	12.33	2.98	11.10	2.63
RAVLT Total	58.06	8.35	52.89	9.35
Delayed	12.87	2.59	11.25	3.48
Rey-O Recall	22.87	5.57	20.18	5.57
RNVLT Total	43.90	11.55	40.43	11.36
Delayed	11.03	3.41	9.86	3.32
CCC Trigrams	48.03	5.99	46.04	5.92
Visuoperceptual				
Visual Search*	124.75	31.01	146.88	67.79
Facial Recogn.	46.55	3.28	46.50	2.97
Hooper VOT	28.02	1.75	27.73	2.28
Rey-O Copy	32.84	1.90	32.68	1.89
R-L Orientation	31.61	0.80	30.79	2.25

* Scores represent units of time

Table 6.15 (Continued)

Neuropsychological Profile of Groups by Health Status

(N = 59)

Tests	Healthy (n = 31) Mean	SD	Nonhealthy (n = 28) Mean	SD
Language				
Word Fluency	47.42	12.44	43.89	10.80
Boston Naming	78.13	9.02	78.04	5.55
Token Test	77.26	1.09	77.43	0.92
Tactile				
Tactile Form Pref.	9.77	0.56	9.50	0.92
Nonp.	9.74	0.63	9.68	0.98
Time Pref.*	67.68	32.15	77.61	38.91
Nonp.*	84.10	37.10	86.86	44.45
Finger Loc. Pref.	29.10	1.14	28.68	1.66
Nonp.	29.06	1.29	28.36	2.00
Motor				
Dynamometer Pref.	44.54	7.01	37.64	7.49
Nonp.	39.92	6.61	34.63	6.73
Finger Tap. Pref.	60.70	5.93	55.49	5.70
Nonp.	54.25	5.35	50.77	6.66
Lateral Dominance	13.13	1.08	12.11	3.41

* Scores represent units of time

HYPOTHESIS 1: Nonhealthy participants will achieve lower scores than members of the Healthy groups. In view of the absence of HIV-related symptomatology, the latter groups (HIV- & HIV+) are expected to display comparable levels of performance.

The omnibus F tests performed on the mean raw and factor scores disclosed a significant health status effect ($p = .024$, $p = .002$ respectively) confirming the first hypothesis. Tables 6.16 and 6.17 contain the results of these analyses. Univariate F tests demonstrated that the verbal IQ, the Rey Auditory Verbal Learning Test, and the motor tests (Dynamometer and Finger Tapping) contributed to the overall health status effect. Similarly, factors 3 and 5 constituted the relevant unique dimensions which correspond to verbal/language-related skills, grip strength and fine motor speed.

Auxiliary analyses (Table 6.18 & 6.19) compared both healthy groups (HIV- & HIV+) and produced overall F tests which indicated no group differences between these individuals on raw data and factor scores ($p = .902$, $p = .932$ respectively). Univariate F tests also consistently rejected the presence of group differences on all measures of the neuropsychological test battery and the underlying factorial dimensions.

Table 6.16

Statistical Analysis of Hypothesis 1: Neuropsychological Data of Groups Defined by Health Status (Raw Scores)

(N = 59)

HYPOTHESIS 1: Healthy vs Nonhealthy

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.42272	2.11051	22.00	34.00	.024

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Trail Making	3.05847	.086
PASAT Total	2.07793	.155
Stereognosis	0.39453	.533
Visual Search	2.42195	.125
RNVLT Total	1.17182	.284
Rey-O. Recall	3.12757	.083
RAVLT Total	4.92945	.031
Stories Recall	2.62365	.111
CCC Total	1.56087	.217
F. Tapping Pref.	11.99612	.001
F. Tapping Nonp.	4.84070	.032
Dynamometer Pref.	13.82736	.000
Dynamometer Nonp.	9.43990	.003
Verbal IQ	6.89317	.011
Word Fluency	1.22717	.273
Boston Naming	0.00194	.965
Token Test	0.48755	.488
Performance IQ	2.06965	.156
Face Recognition	0.00092	.976
Hooper VOT	0.35349	.555
R-L Orientation	3.61785	.062
Finger Localization	2.42634	.125

Table 6.17

**Statistical Analysis of Hypothesis 1:
Neuropsychological Data of Groups
Defined by Health Status (Factor Scores)**

(N = 59)

HYPOTHESIS 1: Healthy vs Nonhealthy

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.66733	4.15422	6.00	50.00	.002

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Neuropsych. Factor 1	1.45837	.232
Neuropsych. Factor 2	1.69156	.199
Neuropsych. Factor 3	4.50950	.038
Neuropsych. Factor 4	0.24568	.622
Neuropsych. Factor 5	13.86733	.000
Neuropsych. Factor 6	0.00879	.926

Table 6.18

Statistical Analysis of the Neuropsychological Data for HIV- and HIV+ Groups (Raw Scores)

(N = 31)

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.27617	0.58967	22.00	34.00	.902

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Trail Making	0.96726	.330
PASAT Total	1.27798	.263
Stereognosis	0.74307	.392
Visual Search	1.73953	.193
RNVLT Total	1.25359	.268
Rey-O. Recall	0.88848	.350
RAVLT Total	0.04205	.838
Stories Recall	0.21004	.649
CCC Total	1.49562	.227
F. Tapping Pref.	0.79400	.377
F. Tapping Nonp.	0.06859	.794
Dynamometer Pref.	0.41758	.521
Dynamometer Nonp.	0.64247	.426
Verbal IQ	1.86685	.177
Word Fluency	0.54562	.463
Boston Naming	0.00144	.970
Token Test	0.84677	.361
Performance IQ	1.40647	.241
Face Recognition	0.17382	.678
Hooper VOT	0.72639	.398
R-L Orientation	0.09271	.762
Finger Localization	0.00114	.973

Table 6.19

Statistical Analysis of the Neuropsychological Data for HIV- and HIV+ Groups (Factor Scores)

(N = 31)

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.96476	0.30435	6.00	50.00	.932

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Neuropsych. Factor 1	0.25500	.616
Neuropsych. Factor 2	0.29345	.590
Neuropsych. Factor 3	0.08436	.773
Neuropsych. Factor 4	1.12891	.293
Neuropsych. Factor 5	0.31747	.575
Neuropsych. Factor 6	0.04892	.826

Simple statistics for groups defined by medical diagnosis are presented in Table 6.20. Means and standard deviations of the WAIS-R subtests are available in Appendix E-3. A cursory review of the table suggests that all mean scores follow the expected direction. Analyses verifying statistical group differences based on medical diagnosis were conducted using MANOVA (Wilk's criterion) and special contrast vectors in order to test the specific hypotheses stated below.

HYPOTHESIS 2: The AIDS group will display a poorer neuropsychological profile than that of the ARC, HIV+, and HIV- groups.

The outcome of this analysis (Table 6.21) only approached a significant group effect ($p = .089$). Power of the test may have been compromised by the reduced sample size (Siegel, 1956; Winer, 1971) when examining the participants according to their medical diagnostic classification. As committing Type I errors was considered less critical than rendering Type II errors, the results of the univariate F tests were reviewed for the purpose of determining which tests may contribute to producing an overall group effect. These could then represent the focus of investigations in subsequent studies. Groups effects were thus noted on Trail Making, Dynamometer (both hands), Verbal IQ, Performance IQ, and Finger Localization. Pairwise comparisons were executed

Table 6.20

Neuropsychological Profile of Groups by Medical Diagnosis

(N = 59)

Tests	HIV- (n = 17) Mean	SD	HIV+ (n = 14) Mean	SD	ARC (n = 14) Mean	SD	AIDS (n = 14) Mean	SD
Cognitive								
FSIQ	116.65	9.05	110.93	11.57	109.57	12.77	105.14	11.18
VIQ	116.94	10.70	111.57	10.44	108.36	12.02	105.21	10.36
PIQ	112.53	10.39	107.71	11.72	109.07	11.18	102.71	11.84
Attention/Concentration								
PASAT 2.4"	44.76	10.62	40.57	9.42	40.36	11.47	37.00	7.51
2.0"	40.41	12.28	36.00	10.60	36.36	9.94	33.00	8.68
1.6"	36.59	10.01	31.36	9.85	29.21	6.80	28.71	7.26
1.2"	27.18	7.95	23.79	8.08	21.07	5.88	23.43	4.75
Total Time*	12.57	3.86	14.06	3.66	14.73	4.15	14.66	2.79
Trail A*	25.88	10.17	26.21	7.69	29.71	8.61	33.14	11.01
Trail B*	55.59	20.81	68.50	28.66	62.79	13.73	84.64	49.27
Memory								
Stories Imm.	13.68	3.10	13.23	3.42	13.04	3.19	11.93	2.03
Del.	12.54	3.11	12.07	2.91	11.39	3.08	10.80	2.18
RAVLT Total	57.76	8.97	58.43	7.86	53.86	7.56	51.93	11.06
Delayed	12.59	2.98	13.21	2.08	10.71	3.34	11.79	3.66
Rey-O Recall	23.73	5.70	21.82	5.42	20.11	4.40	20.25	6.72
RNVLT Total	46.00	11.88	41.36	11.01	39.00	9.03	41.86	13.49
Delayed	11.82	3.15	10.07	3.58	9.29	2.87	10.43	3.74
CCC Trigrams	49.18	5.71	46.64	6.23	43.64	5.81	48.43	5.16
Visuoperceptual								
Vis. Search*	113.68	27.04	138.20	31.04	137.66	34.53	156.11	90.39
Fac. Recogn.	46.76	3.25	46.29	3.43	46.14	3.37	46.86	2.60
Hooper VOT	27.73	1.98	28.36	1.42	28.14	1.36	27.32	2.93
Rey-O Copy	32.94	1.34	32.71	2.40	32.71	1.77	32.64	2.06
R-L Orient.	31.53	1.01	31.71	0.47	30.71	2.61	30.86	1.92

* Scores represent units of time

Table 6.20 (Continued)

Neuropsychological Profile of Groups by Medical Diagnosis

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Tests	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Language								
Word Fluency	48.82	11.76	45.71	13.46	41.00	8.79	46.79	12.12
Naming	78.18	9.86	78.07	8.25	79.29	4.44	76.79	6.39
Token	77.41	0.87	77.07	1.33	77.50	0.65	77.36	1.15
Tactile								
T. Form Pref.	9.82	0.53	9.71	0.61	9.71	0.82	9.29	0.99
Nonp.	9.76	0.75	9.71	0.47	10.00	0.00	9.36	1.34
Time Pref.	67.41	37.46	68.00	25.64	72.29	33.49	82.93	44.29
Nonp.	74.41	40.51	95.86	29.74	69.21	20.06	104.36	55.06
F. Loc. Pref.	29.06	1.09	29.14	1.23	28.77	1.42	28.57	1.91
F. Loc. Nonp.	29.12	1.32	29.00	1.30	29.00	1.30	27.71	2.40
Motor								
Dynam. Pref.	45.28	7.07	43.64	7.11	40.70	6.81	34.59	7.07
Nonp.	40.76	6.83	38.89	6.43	37.32	4.82	31.95	7.42
F. Tap. Pref.	59.85	7.00	61.73	4.32	54.63	5.45	56.36	6.01
Nonp.	53.99	5.69	54.57	5.09	50.94	5.66	50.60	7.75
Lateral Dom.	13.12	1.11	13.14	1.08	12.46	3.32	11.75	3.58

* Scores represent units of time

Table 6.21

Statistical Analysis of Hypothesis 2: Neuropsychological Data of the AIDS Group Versus all Other Groups (Raw Scores)

(N = 59)

HYPOTHESIS 2: AIDS vs HIV-, HIV+, ARC

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.48149	1.66425	22.00	34.00	.089

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HDS
Trail Making	6.09780	.017	HIV- < AIDS
PASAT Total	0.61078	.438	---
Stereognosis	3.12762	.083	---
Visual Search	2.76998	.102	---
RNVLT Total	0.00554	.941	---
Rey-O. Recall	0.90331	.346	---
RAVLT Total	2.99463	.089	---
Stories Recall	1.87653	.176	---
CCC Total	1.21865	.274	---
F. Tapping Pref.	1.75991	.190	---
F. Tapping Nonp.	1.88603	.175	---
Dynamometer Pref.	16.06928	.000	HIV-, HIV+ > AIDS
Dynamometer Nonp.	12.63793	.001	HIV-, HIV+ > AIDS
Verbal IQ	4.49924	.038	HIV- > AIDS
Word Fluency	0.20217	.655	---
Boston Naming	0.54083	.465	---
Token Test	0.00878	.926	---
Performance IQ	4.19386	.045	---
Face Recognition	0.22193	.639	---
Hooper VOT	1.49418	.227	---
R-L Orientation	0.80432	.374	---
Finger Localization	4.27649	.043	---

using Tukey's Honestly Significant Difference (HSD). From these, the AIDS patient group was not found to be significantly different than all three other groups taken together on any of the measures. However, they revealed a weaker grip strength (both hands) than both Healthy groups (HIV- & HIV+); and performed less well than the HIV- group on Verbal IQ and Trail Making.

The results of this comparison vector on the factor scores is much stronger ($p = .007$), and revealed a notable decrease in the performance levels of the AIDS group versus all three remaining ones (Table 6.22). The critical dimensions identified by the univariate F tests involved cognitive processing speed (factor 1), verbal/language-related skills (factor 3), and motor strength (factor 3). Tukey's HSD replicated this pattern of group performance for factor 3 but suggested that the AIDS group was slower than the HIV- and ARC groups only for the time factor.

HYPOTHESIS 3: Univariate differences are predicted between the ARC and the healthy groups (HIV- & HIV+) on the most taxing tests only, such as the Consonant Trigrams and the PASAT. Overall group differences are not expected between ARC and AIDS groups in view of an overlap of impaired performance.

Table 6.22

Statistical Analysis of Hypothesis 2: Neuropsychological Data of the AIDS Group Versus all Other Groups (Factor Scores)

(N = 59)

HYPOTHESIS 2: AIDS vs HIV-, HIV+, ARC

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.70902	3.41990	6.00	50.00	.007

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F	Tukey HSD
Neuropsych. Factor 1	4.79013	.038	
Neuropsych. Factor 2	0.02831	.867	
Neuropsych. Factor 3	7.85090	.007	HIV- > AIDS
Neuropsych. Factor 4	2.08505	.154	
Neuropsych. Factor 5	2.95725	.091	
Neuropsych. Factor 6	0.13778	.712	

From the univariate F tests, varying performance levels were noted on Consonant Trigrams and Finger Tapping (dominant hand) (Table 6.23). The results of the pairwise comparisons indicated that ARC patients obtained lower scores than the HIV- group on Consonant Trigrams, and slower Finger Tapping ratings than HIV+ individuals. Hypothesis 3 was thus corroborated only partially with respect to Consonant Trigrams but not with the PASAT. The omnibus F test comparing the ARC group to the healthy ones (HIV- & HIV+) on the whole test battery indicated no significant difference between the groups (p = .127). A supplementary analysis (Table 6.24) indicated no overall group effect between the ARC and the AIDS groups (p = .380). However, univariate F tests suggested significant group differences between the two patient groups on a few measures: while ARC patients were poorer in performance than AIDS patients on Consonant Trigrams, they were nevertheless stronger than this group with respect to grip strength, bilaterally.

Analogous group comparisons based on the factor scores (Table 6.25) revealed a significant overall F effect between the ARC and healthy groups (p = .019), with fine motor speed (factor 5) as the critical underlying dimension accounting for the discrepancy in the mean factor scores (univariate F and Tukey's HSD). There was also a tendency (p = .065) for the AIDS patients to perform differently than the ARC individuals on factors 1, 3, and 4 (Table 6.26).

Table 6.23

**Statistical Analysis of Hypothesis 3:
Neuropsychological Data of the ARC Group
Versus both Healthy Groups**

(N = 45)

HYPOTHESIS 3: ARC vs HIV- & HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.50138	1.53696	22.00	34.00	.127

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HDS
Trail Making	0.13419	.716	---
PASAT Total	1.42864	.237	---
Stereognosis	0.24655	.621	---
Visual Search	0.49814	.483	---
RNVLT Total	1.59441	.212	---
Rey-O. Recall	2.16784	.147	---
RAVLT Total	2.14816	.148	---
Stories Recall	0.98558	.325	---
CCC Total	5.31292	.025	HIV- > ARC
F. Tapping Pref.	10.65734	.002	HIV+ > ARC
F. Tapping Nonp.	2.87548	.096	---
Dynamometer Pref.	2.76777	.102	---
Dynamometer Nonp.	1.44388	.235	---
Verbal IQ	2.82267	.099	---
Word Fluency	2.77811	.101	---
Boston Naming	0.22124	.640	---
Token Test	0.61141	.438	---
Performance IQ	0.08384	.773	---
Face Recognition	0.13873	.711	---
Hooper VOT	0.02197	.883	---
R-L Orientation	2.79853	.100	---
Finger Localization	0.17634	.676	---

Table 6.24

Supplementary Statistical Analysis of the Neuropsychological Data of the ARC and AIDS Groups (Raw Scores)

(N = 28)

HYPOTHESIS 3: ARC vs AIDS

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.58109	1.11413	22.00	34.00	.380

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HDS
Trail Making	3.21483	.078	---
PASAT Total	0.00216	.963	---
Stereognosis	2.94380	.092	---
Visual Search	0.89764	.348	---
RNVLT Total	0.43285	.513	---
Rey-O. Recall	0.00451	.947	---
RAVLT Total	0.32360	.572	---
Stories Recall	0.29763	.588	---
CCC Total	4.86539	.032	HIV- > ARC
F. Tapping Pref.	0.61103	.438	---
F. Tapping Nonp.	0.02206	.882	---
Dynamometer Pref.	5.30201	.025	HIV-, HIV+ > AIDS
Dynamometer Nonp.	4.83006	.032	HIV-, HIV+ > AIDS
Verbal IQ	0.58309	.448	---
Word Fluency	1.72256	.195	---
Boston Naming	0.74575	.392	---
Token Test	0.13603	.714	---
Performance IQ	2.23522	.141	---
Face Recognition	0.35244	.555	---
Hooper VOT	1.15664	.287	---
R-L Orientation	0.05048	.823	---
Finger Localization	2.06545	.156	---

Table 6.25

Supplementary Statistical Analysis of the Neuropsychological Data for ARC and Healthy Groups (Factor Scores)

(N = 45)

HYPOTHESIS 3: ARC vs HIV- & HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.74681	2.82531	6.00	50.00	.019

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Neuropsych. Factor 1	0.00837	.927	
Neuropsych. Factor 2	2.13427	.150	
Neuropsych. Factor 3	0.34200	.561	
Neuropsych. Factor 4	2.66079	.109	
Neuropsych. Factor 5	10.89636	.002	HIV-, HIV+ > ARC
Neuropsych. Factor 6	0.02265	.881	

Table 6.26

Supplementary Statistical Analysis of the Neuropsychological Data for ARC and AIDS Groups (Factor Scores)

(N = 28)

HYPOTHESIS 3: ARC vs AIDS

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.79561	2.14087	6.00	50.00	.065

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Neuropsych. Factor 1	3.33377	.073
Neuropsych. Factor 2	0.48246	.490
Neuropsych. Factor 3	3.75684	.058
Neuropsych. Factor 4	4.40208	.041
Neuropsych. Factor 5	0.23410	.630
Neuropsych. Factor 6	0.14935	.701

Supplementary Analyses

Discrimination of group differences based upon measures of central tendency often tend to camouflage individual impairments. Reitan and Boll (1973) suggested that a person's performance be rated as normal or abnormal by using a composite score of all tests administered. Hence, Grant and his collaborators (Grant, et al., 1987) classified their subject's performance individually on each test as unimpaired, probably impaired, or definitely impaired. If at least one test score was considered definitely impaired, or at least two test scores were rated probably impaired, the neuropsychological profile as a whole was deemed atypical and/or abnormal. Following this system, the overall neuropsychologic status of the current study sample was classified as normal or abnormal, using criteria compatible with those of Grant and his collaborators (1987). Probable impairment was defined as :

1) a scaled score of 6 on one of the subtests of the WAIS-R;
2) a 25-30% loss of information after a 30-minute delayed recall of verbal or visual material;
3) a percentile rank of 9-16, and/or a score ranking 1.0 to 1.3 standard deviation below the mean in normative data.

Criteria for definite impairment were:

1) a scaled score of 5 or less on one of the subtests of the WAIS-R;
2) more than a 30% loss of information after a 30-minute delayed recall of verbal or visual material;
3) a percentile rank below 9, and/or a score ranking more than 1.3 standard deviation below the mean in normative data.

The outcome of this global classification of neuropsychologic status yielded the following findings: 5 of 17 HIV-, 6 of 14 HIV+, 8 of 14 ARC, and 8 of 14 AIDS were considered to have an overall abnormal profile. The findings are not consistant with the results reported by Grant and his colleagues (1987). The distribution of abnormality was not statistically diffent between the healthy and the nonhealthy groups ($\underline{Chi}^2(1) = 1.38$, $\underline{p} > .20$). The proportion of patients with neuropsychological dysfunction thus ranged from 29.4% (HIV-) to 42.9% (HIV+) in the healthy groups. The ARC and AIDS groups both demonstrated 57.1% of atypical neuropsychologic performance.

In view of the lengthy and time consuming nature of the neuropsychological test battery, exploratory analyses were conducted according to the types of cerebral functions assessed. Tests were divided along the following performance areas: verbal, nonverbal, memory, divided and

sustained attention/concentration, and sensorimotor tasks. Table 6.2/ demonstrates the results of the MANOVAs conducted on these specific function areas for all of the hypotheses stated above. In summary, the AIDS group was found to be definitely different from the remaining three groups on the sensorimotor tests (p = .004) only. Measures of attention/concentration (p = .053) may contribute to the discrimination of the AIDS from the ARC groups, while sensorimotor tests (p = .061) only suggested group differences between the two. Healthy groups (HIV- & HIV+) appear to have better verbal cognitive skills than the ARC patients (p = .053). Finally, the healthy groups (HIV- & HIV+) appeared to be equivalent on all functional areas.

Personality and Emotional Aspects

The second aim of this study was to provide a quantitative evaluation of the emotional and psychosocial repercussions associated with HIV infection. The findings related to this area are discussed in this section. Statistical analyses verified specific a priori hypotheses regarding group differences on three measures of emotional functioning: a personality inventory (MMPI), a profile of behavioural dysfunction associated with illness (SIP), and indices of anxiety (STAI).

Table 6.27

Statistical Analyses of the Neurospychological Functional Areas for Each Hypothesis

Significance of Multivariate F Tests

Tests	HIV- vs HIV+	ARC vs AIDS	ARC vs HIV- & HIV+	AIDS vs ARC, HIV- & HIV+
Verbal	.610	.368	.053	.150
Nonverbal	.359	.316	.984	.130
Memory	.481	.419	.519	.308
Attention	.449	.053	.106	.130
Sensorimotor	.550	.061	.056	.004

Total Sample

The raw scores of the MMPI scales are transformed into T-scores (M = 50; SD = 10). As a general practice, a T-score of 70 (= 2 SD) and above is considered a high score, and suggestive of dysfunction. Table 6.28 contains descriptive statistics of the MMPI profiles. All were considered valid and interpretable (L < 53.3 , F < 59.8, K < 49.0; n = 59). Means, standard deviations, and range of scores (minimum, maximum) are listed for all subscales. In comparing the standard deviations to the normative value of 10, more variability was noted for Hysteria, Hypochondriasis and Depression subscales. T-score conversions above 70 typically denote significant dysfunction. For the total sample, Masculinity-Femininity was the only scale which surpassed the cut-off score, reflecting the sexual orientation of the sample.

On the SIP, the weights of endorsed items are summed and divided by the total potential score for each given subscale, yielding scores which reflect the degree of impairment for a particular subscale or a composite dimension. Simple statistics of the SIP subscales and composite scores are tabulated in Table 6.29. Noteworthy, is the degree of variability within all subscales of the SIP. All standard deviations were greater than the actual mean scores. Nevertheless, elevations were noted particularly with most psychosocial subscales (Alert

Table 6.28

MMPI Profile Scores of the Total Sample

(N = 59)

Subscales	Mean	SD	Minimum	Maximum
L	53.39	10.45	26.00	75.00
F	59.85	11.80	23.00	82.00
K	49.00	11.19	26.00	69.00
Hypochondriasis	60.36	13.48	30.00	85.00
Depression	64.88	12.05	36.00	87.00
Hysteria	62.76	15.60	30.00	86.00
Psychopathic Deviat	58.71	11.92	30.00	86.00
Masculinity-Femininity	71.59	6.71	58.00	88.00
Paranoia	56.81	11.18	26.00	86.00
Psychasthenia	61.64	11.39	40.00	85.00
Schizophrenia	62.49	9.62	41.00	86.00
Hypomania	58.25	9.98	38.00	79.00
Social Introversion	51.14	11.11	27.00	69.00

Table 6.29

SIP Profile Scores of the Total Sample

(N = 59)

Subscales	Mean	SD	Minimum	Maximum
Sleep & Rest	21.87	25.04	0.00	100.00
Emotional Behaviour	19.42	24.02	0.00	90.00
Body Care & Movement	3.41	6.10	0.00	26.00
Home Management	9.05	15.29	0.00	61.00
Mobility	5.32	9.80	0.00	51.00
Social Interaction	15.73	16.90	0.00	61.00
Ambulation	5.21	8.25	0.00	37.00
Alert Behaviour	20.90	29.83	0.00	92.00
Communication	6.23	12.31	0.00	48.00
Work	24.95	29.65	0.00	70.00
Recreation & Pastimes	21.25	24.71	0.00	80.00
Eating	2.97	4.71	0.00	19.00
Physical	3.93	6.16	0.00	26.23
Psychosocial	17.03	19.38	0.00	65.65
Total	15.58	16.63	0.00	55.05

Behaviour, Emotional Behaviour, and Social Interaction), and those scales germane to basic life activities (Work, Recreation & Pastimes, and Sleep & Rest). In contrast, the physical subscales (Body Care & Movement, Mobility, Ambulation, and Eating) appeared less extensively affected.

On the STAI, the weights of endorsed items are summed and translated into a T-score. Percentile ranks are also available. Table 6.30 illustrates the descriptive statistics of the STAI. Mean T-scores of State and Trait anxiety seem comparable and suggest only a slightly higher level of anxiety experienced in everyday life than at the time of the evaluation.

In order to reduce the data set and identify underlying dimensions, two Principal Component Analyses with varimax rotation were conducted on the MMPI and SIP each. Table 6.31 presents the results of this analysis on the MMPI. Three factors emerged with an eigenvalue > 1.0, accounting for 77% of the variance:

Factor 1: Loadings > .7 on Hypochondriasis, Hysteria, Depression, and Schizophrenia.

Factor 2: Loadings > .7 on Paranoia and Masculinity-Femininity.

Factor 3: Loadings > .7 on Social Introversion.

Based on the MMPI, there are three underlying dimensions which depict the psychological aspects of HIV infection for the total sample: 1) an indication of dysfunction including

Table 6.30

STAI Scale Scores of the Total Sample

(N = 59)

Scales	Mean	SD	Minimum	Maximum
State Anxiety	51.54	10.36	26.00	77.00
Trait Anxiety	55.68	10.65	26.00	79.00

Table 6.31

PCA of the MMPI

(N = 59)

Final Statistics

Factor	Eigenvalue	Pct of Var	Cum Pct
1	4.74560	47.5	47.5
2	1.67184	16.7	64.2
3	1.09393	10.9	75.1

Loadings of the Rotated Factor Matrix

Scales	Factor 1	Factor 2	Factor 3
Hypochondriasis	.944	.037	-.008
Depression	.723	.183	.531
Hysteria	.883	.169	-.088
Psychopathic Deviate	.496	.555	-.323
Masculinity-Femininity	.064	.746	.124
Paranoia	.199	.785	.081
Psychasthenia	.651	.452	.443
Schizophrenia	.719	.489	.213
Hypomania	.409	.201	-.673
Social Introversion	.232	.173	.834

complaints of somatic, affective, and ideational nature; 2) the sexual identity and personal characteristics of the population at risk; and 3) the degree of social interaction. (Mild elevations [T-score = 55 to 65] on the Paranoia scale usually describe individuals in a positive light [Graham, 1977]).

The PCA with varimax rotation of the SIP subscales generated two factors with eigenvalues > 1.0, and accounted for 74% of the variance (Table 6.32).

Factor 1: Loadings > .7 on Home Management, Ambulation, Mobility, Body Care & Movement, and Recreation & Pastimes.

Factor 2: Loadings > .7 on Emotional Behaviour, Alert Behaviour, Social Interaction, and Communication.

Based on the SIP, two principal dimensions underlie the psychological aspects associated with HIV infection in this sample of participants. The first factor represents the physical well being and activity related functioning. The second one corresponds in an identical fashion to the psychosocial dimension of the SIP.

Group Comparisons

Simple statistics of the MMPI, SIP, and STAI are summarized in Tables 6.33 to 6.35, respectively. The Healthy group achieved lower mean scores than the Nonhealthy group on all of the listed subscales, except for

Table 6.32

PCA of the SIP

(N = 59)

Final Statistics

Factor	Eigenvalue	Pct of Var	Cum Pct
1	7.75025	64.6	64.6
2	1.09848	9.2	73.7

Loadings of the Rotated Factor Matrix

Subscales	Factor 1	Factor 2
Sleep & Rest	.612	.672
Emotional Behaviour	.127	.888
Body Care & Movement	.805	.268
Home Management	.868	.200
Mobility	.817	.333
Social Interaction	.489	.729
Ambulation	.822	.284
Alert Behaviour	.443	.736
Communication	.300	.701
Work	.687	.360
Recreation & Pastimes	.744	.481
Eating	.659	.508

Table 6.33

MMPI Profile Scores of Groups by Health Status

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
Subscales	**Mean**	**SD**	**Mean**	**SD**
L	54.35	8.31	52.21	12.47
F	56.97	11.15	63.04	11.86
K	51.64	10.55	46.07	11.34
Hypochondriasis	52.03	9.65	69.57	10.94
Depression	59.64	10.38	70.68	11.20
Hysteria	54.06	11.25	72.39	14.11
Psychopathic Deviate	56.68	11.68	60.96	11.99
Masculinity-Femininity	72.29	6.95	70.82	6.47
Paranoia	55.84	12.89	57.89	9.02
Psychasthenia	57.45	10.54	66.29	10.63
Schizophrenia	58.77	8.31	66.61	9.42
Hypomania	55.93	10.62	60.82	8.70
Social Introversion	48.93	10.84	53.57	11.09

Table 6.34

SIP Profile Scores of Groups by Health Status

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
Subscales	**Mean**	**SD**	**Mean**	**SD**
Sleep & Rest	5.46	12.00	40.03	23.16
Emotional Behaviour	8.61	14.21	31.39	27.07
Body Care Movement	0.60	2.17	6.51	7.46
Home Management	0.69	3.83	18.31	17.79
Mobility	0.61	3.38	10.54	11.82
Social Interaction	5.41	9.57	27.16	15.93
Ambulation	0.53	2.96	10.39	9.15
Alert Behaviour	4.83	16.12	38.70	31.60
Communication	1.80	5.78	11.12	15.53
Work	3.37	10.17	48.83	25.45
Recreation & Pastimes	5.47	14.03	38.71	22.16
Eating	0.36	1.42	5.86	5.38
Physical	0.49	2.36	7.74	6.82
Psychosocial	5.65	11.08	29.64	18.89
Total	3.76	7.95	28.67	13.63

Table 6.35

STAI Scale Scores of Groups by Health Status

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
Scales	**Mean**	**SD**	**Mean**	**SD**
State Anxiety	48.71	9.67	54.68	10.36
Trait Anxiety	53.32	10.04	58.29	10.88

Masculinity-Femininity. The Nonhealthy group showed greater variability in performance level than the Healthy group on the MMPI and the SIP, as indicated by the higher values of the standard deviations. Profiles of the MMPI and SIP for each health status groups are depicted in Figures 6.1 and 6.2. Statistical differences based on health status were determined by MANOVAs, using Wilk's criterion. The two groups were also compared on their total SIP score using a one-way ANOVA.

> **HYPOTHESIS 4:** Nonhealthy groups will display more emotional dysfunction on all three measures of psychological functioning (MMPI SIP, and STAI) than the Healthy ones. No differences between the two healthy groups are expected.

The results of these analyses (Table 6.36 to 6.38) confirmed Hypothesis 4 with respect to the MMPI (p = .0001) and the SIP (p = .0001), whereas the STAI (p = .071) only approached a significant health status effect. Univariate F tests suggested that all of the SIP subscales contributed to the significant health status effect. For the MMPI, scales denoting significant difference between groups were Hypochondriasis, Depression, Hysteria, Psychasthenia, and Schizophrenia. Additional analyses (Tables 6.39 to 6.41) revealed that HIV- and HIV+ groups achieved comparable profiles on the MMPI, SIP, and

Figure 6.1
MMPI Mean Score of Health Status Groups

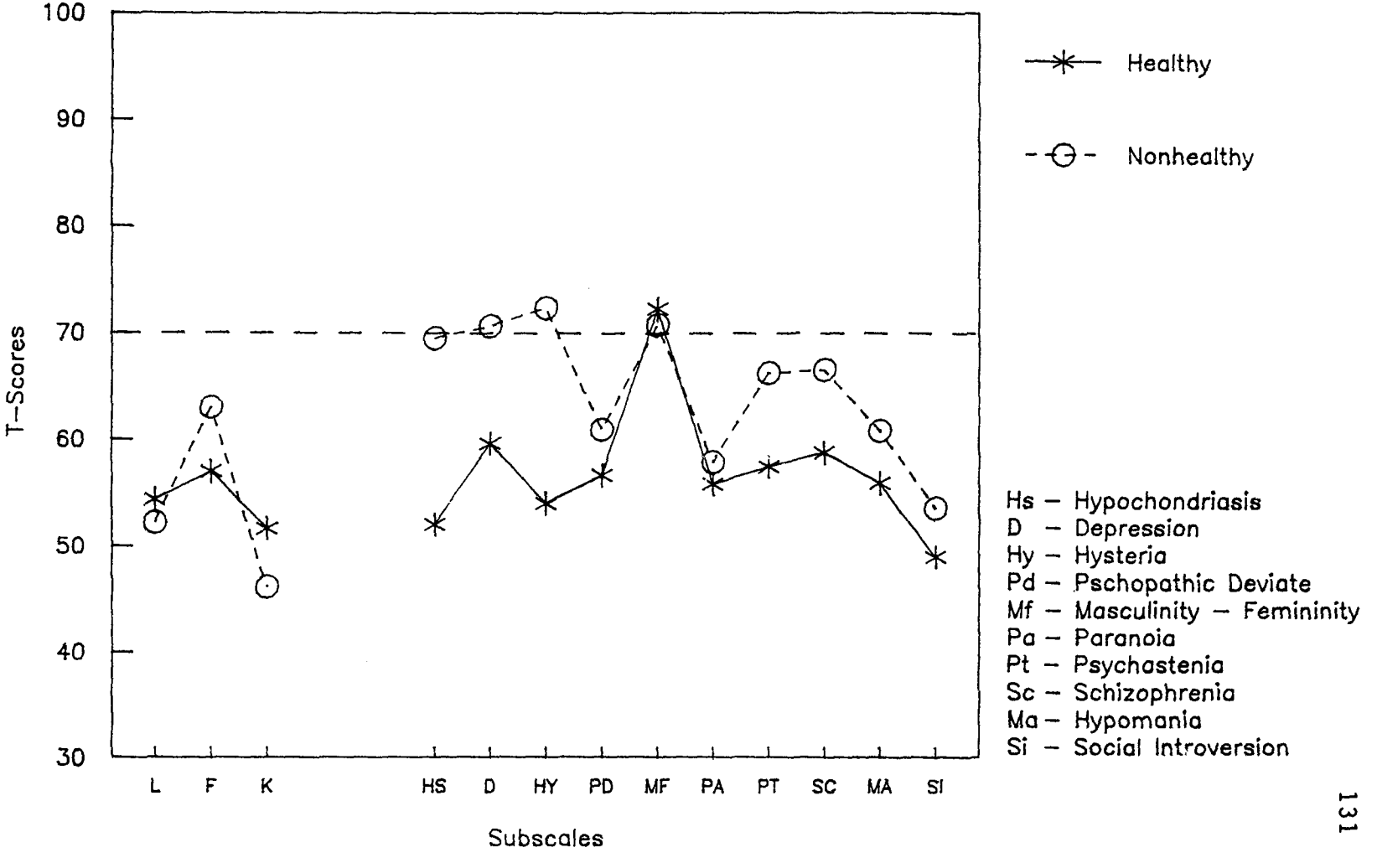


Figure 6.2
SIP Mean Scores of Health Status Groups

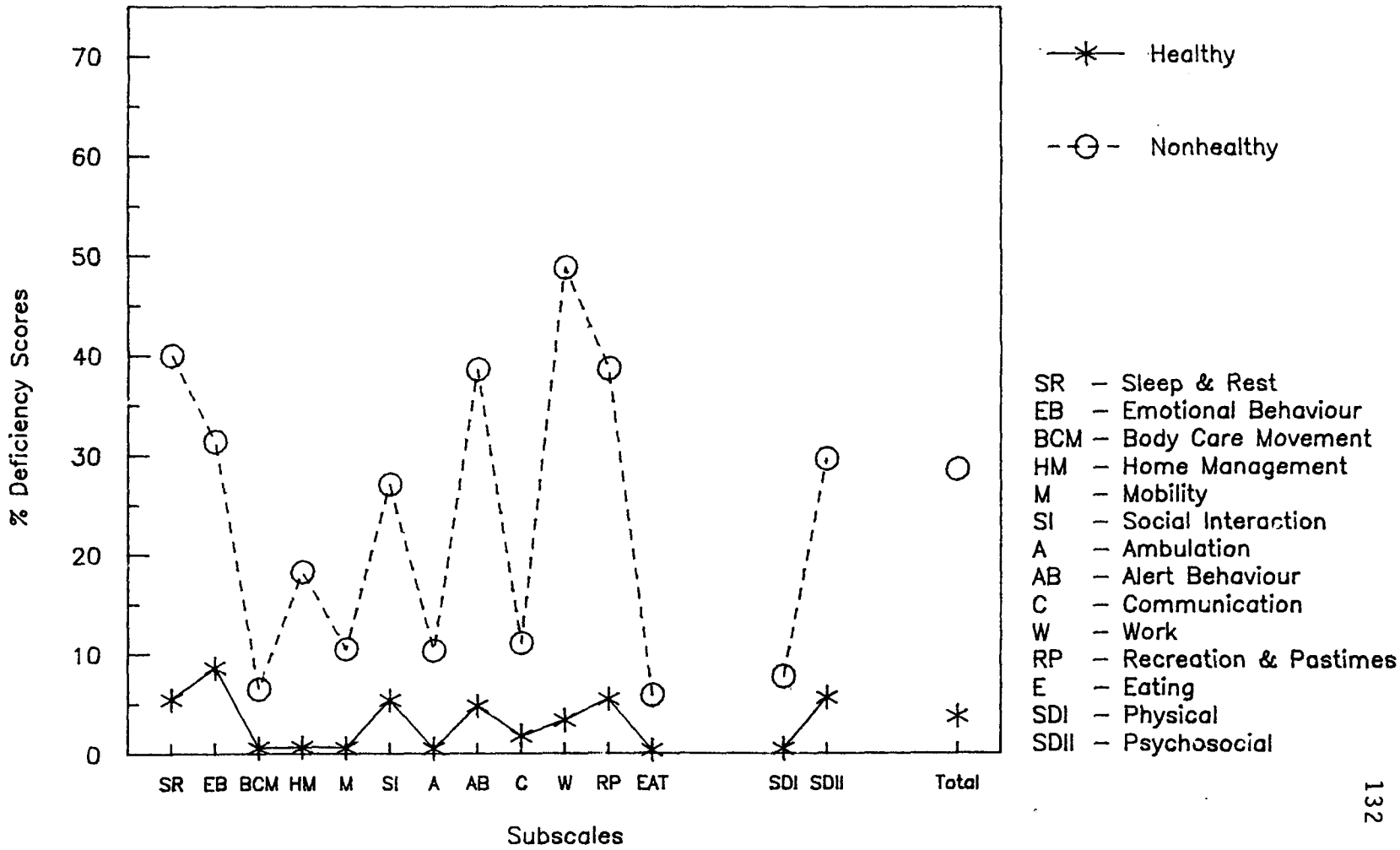


Table 6.36

Statistical Analysis of Hypothesis 4:
MMPI Data of Groups Defined by Health Status

(N = 59)

HYPOTHESIS 4: Healthy vs Nonhealthy

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.44457	5.99683	10.00	48.00	.000

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Hypochondriasis	42.83833	.000
Depression	15.40859	.000
Hysteria	30.70465	.000
Psychopathic Deviate	1.93171	.170
Masculinity-Femininity	0.70062	.406
Paranoia	0.49234	.486
Psychasthenia	10.25217	.002
Schizophrenia	11.51002	.001
Hypomania	3.69081	.060
Social Introversion	2.63230	.110

Table 6.37

Statistical Analysis of Hypothesis 4:
SIP Data of Groups Defined by Health Status

(N = 59)

HYPOTHESIS 4: Healthy vs Nonhealthy

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.27931	9.89090	12.00	46.00	.000

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Sleep & Rest	53.30471	.000
Emotional Behaviour	16.83860	.000
Body Care & Movement	17.78857	.000
Home Management	28.99457	.000
Mobility	20.09629	.000
Social Interaction	41.36645	.000
Ambulation	32.26614	.000
Alert Behaviour	27.67656	.000
Communication	9.70250	.003
Work	84.15545	.000
Recreation & Pastimes	48.31216	.000
Eating	30.05414	.000

Table 6.38

Statistical Analysis of Hypothesis 4:
STAI Data of Groups Defined by Health Status

(N = 59)

HYPOTHESIS 4: Healthy vs Nonhealthy

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.91111	2.73189	2.00	56.00	.074

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
State Anxiety	5.23921	.026
Trait Anxiety	3.32177	.074

Table 6.39

Supplementary Statistical Analysis of the MMPI Data for HIV- and HIV+ Groups

(N = 31)

HIV- vs HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.85385	0.78735	10.00	46.00	.641

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Hypochondriasis	0.09879	.754	---
Depression	0.10411	.748	---
Hysteria	0.71446	.402	---
Psychopathic Deviate	1.44297	.235	---
Masculinity-Femininity	0.55741	.458	---
Paranoia	0.74104	.393	---
Psychasthenia	0.74912	.391	---
Schizophrenia	0.09553	.758	---
Hypomania	0.23815	.627	---
Social Introversion	0.24693	.621	---

Table 6.40

Supplementary Statistical Analysis of the SIP Data for HIV- and HIV+ Groups

(N = 31)

HIV- vs HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.88133	0.49374	12.00	44.00	.907

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
Sleep & Rest	1.455831	.233
Emotional Behaviour	1.00762	.320
Body Care & Movement	1.09310	.300
Home Management	0.56973	.454
Mobility	0.55310	.460
Social Interaction	4.27871	.043
Ambulation	0.86658	.356
Alert Behaviour	2.41275	.126
Communication	1.38086	.245
Work	2.94739	.092
Recreation & Pastimes	2.00980	.162
Eating	0.87654	.353

Table 6.41

Supplementary Statistical Analysis of the STAI Data for HIV- and HIV+ Groups

(N = 31)

HIV- vs HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.97616	0.659 9	2.00	54.00	.521

Univariate F Tests with (1, 57) degrees of freedom

Variables	F Value	Sig. of F
State Anxiety	0.78387	.380
Trait Anxiety	0.02101	.885

STAI measures. All univariate F tests but one (Social Interaction of the SIP) were consistent with this finding. This may represent a spurious group effect. Significance levels are not adjusted for the number of univariate tests performed.

Tables 6.42, 6.43 and 6.44 contain the descriptive statistics of the MMPI, SIP, and STAI respectively, for the four medical diagnostic groups. HIV- and HIV+ displayed lower profile scores on all three measures. Approximately half of the MMPI subscales are mildly more elevated for the ARC group than the AIDS. The ARC patients also obtained greater scores on five subscales of the SIP, while the AIDS patients achieved higher scores on the remaining seven scales. Specific hypothesized group differences based on medical diagnosis were tested using MANOVAs with Wilk's criterion and special contrast vectors.

HYPOTHESIS 5: The AIDS group will display greater profile elevation on the MMPI (Figure 6.3), and report more behavioural dysfunction related to illness on the SIP (Figure 6.4) than the remaining three groups.

Analyses supporting this hypothesis for both the MMPI and the SIP are summarized in Tables 6.45 and 6.46, respectively. Univariate F tests executed on the MMPI subscales indicated that the significant group effect stemmed from the Hypochondriasis and Hysteria scales

Table 6.42

MMPI Profile Scores of Groups by Medical Diagnosis

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Subscales	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
L	51.82	7.32	57.43	8.65	51.43	13.02	53.00	12.34
F	56.88	12.07	57.07	10.38	64.64	13.98	61.43	9.56
K	50.71	11.10	52.79	10.13	41.00	8.50	51.14	11.80
HS	52.23	10.61	51.79	8.73	67.43	12.56	71.71	8.98
D	59.53	11.64	59.79	9.06	71.43	12.77	69.93	9.82
HY	53.06	13.23	55.29	8.60	70.86	16.50	73.93	11.68
PD	54.53	12.59	59.29	10.32	62.50	9.48	59.43	14.28
MF	73.06	6.08	71.36	8.02	71.50	7.72	70.14	5.14
PA	57.47	10.71	53.86	15.33	61.86	8.68	53.93	7.74
PT	59.29	9.20	55.21	11.94	69.50	10.02	63.07	10.58
SC	58.65	7.91	58.93	9.07	66.64	9 74	66.57	9.47
MA	55.35	11.92	56.64	9.19	59.50	6.35	62.14	9.15
SI	50.00	9.72	47.64	12.31	57.71	9.99	49.43	10.90

Table 6.43

SIP Profile Scores of Groups by Medical Diagnosis

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Subscales	Mean	SD	Mean	SD	Mean	SD	Mean	SD
SR	3.29	6.81	8.10	16.17	41.82	24.99	38.24	21.97
EB	6.49	12.61	11.19	16.03	46.42	24.45	16.36	20.92
BCM	0.00	0.00	1.34	3.14	3.42	4.35	9.60	8.73
HM	0.00	0.00	1.52	5.69	10.71	10.94	25.92	20.32
M	0.00	0.00	1.34	5.02	7.81	7.18	13.26	14.93
SI	2.02	4.34	9.52	12.44	30.20	17.10	24.13	14.65
A	0.00	0.00	1.18	4.41	6.66	6.83	14.11	9.86
AB	0.00	0.00	10.70	23.07	42.93	36.42	34.47	26.62
C	0.00	0.00	3.99	8.22	13.84	17.22	8.41	13.73
W	0.63	2.59	6.71	14.44	35.21	26.51	62.46	15.58
RP	2.82	11.62	8.70	16.37	30.05	20.03	47.36	21.39
E	0.00	0.00	0.81	2.06	5.41	5.71	6.31	5.20
Physical	0.00	0.00	1.09	3.49	5.05	4.29	10.43	7.92
Psychosocial	2.33	4.58	9.68	15.02	36.47	21.04	22.80	14.06
Total	1.52	3.10	6.49	10.92	27.36	14.27	29.97	13.37

Table 6.44

STAI Scale Scores of Groups by Medical Diagnosis

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Scales	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
State Anxiety	47.59	11.73	50.07	6.54	59.71	8.57	49.64	9.73
Trait Anxiety	53.76	9.95	52.79	10.49	63.71	8.61	52.86	10.41

Figure 6.3
MMPI Mean Scores of Medical Diagnostic Groups

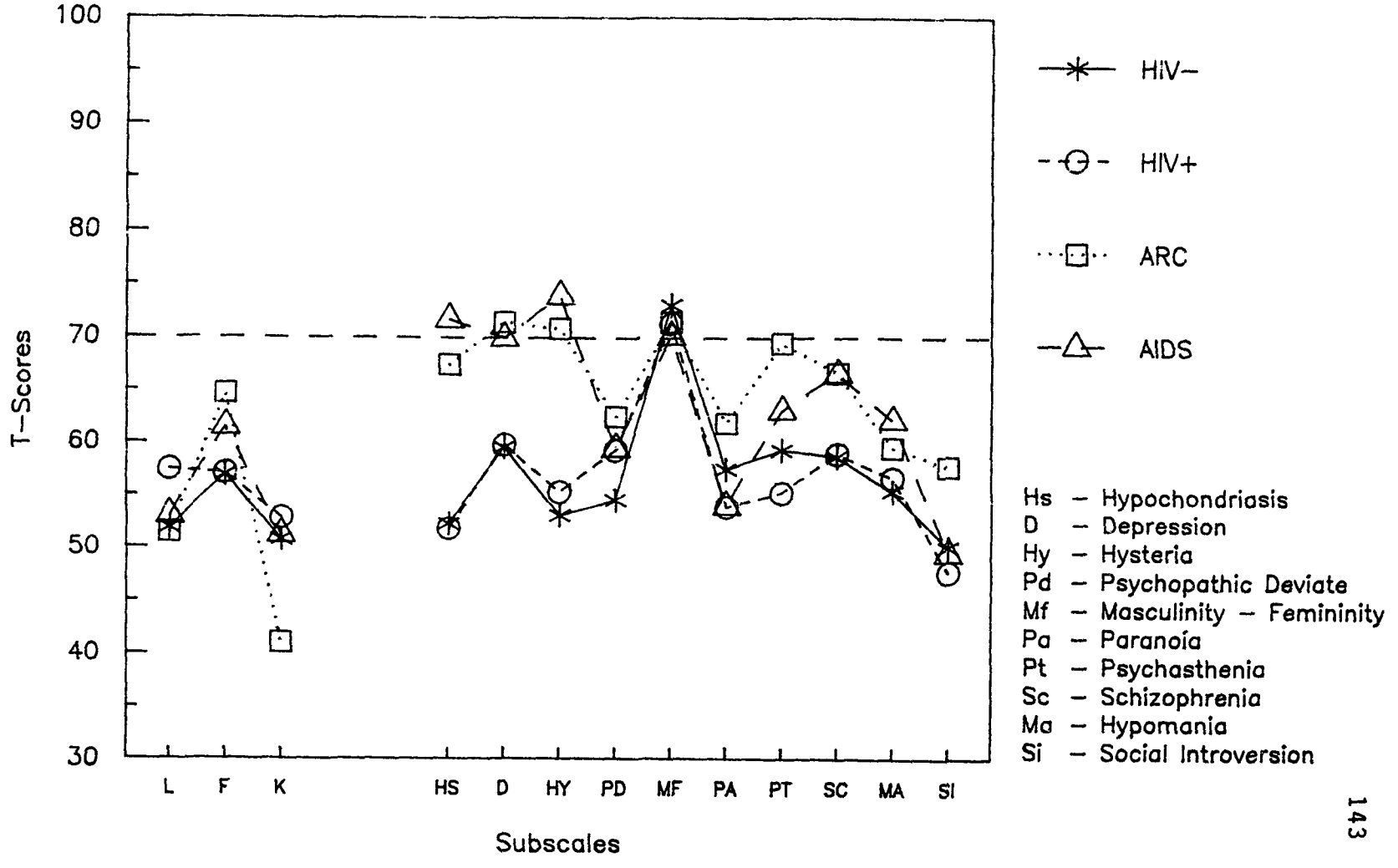


Figure 6.4
SIP Mean Scores of Medical Diagnostic Groups

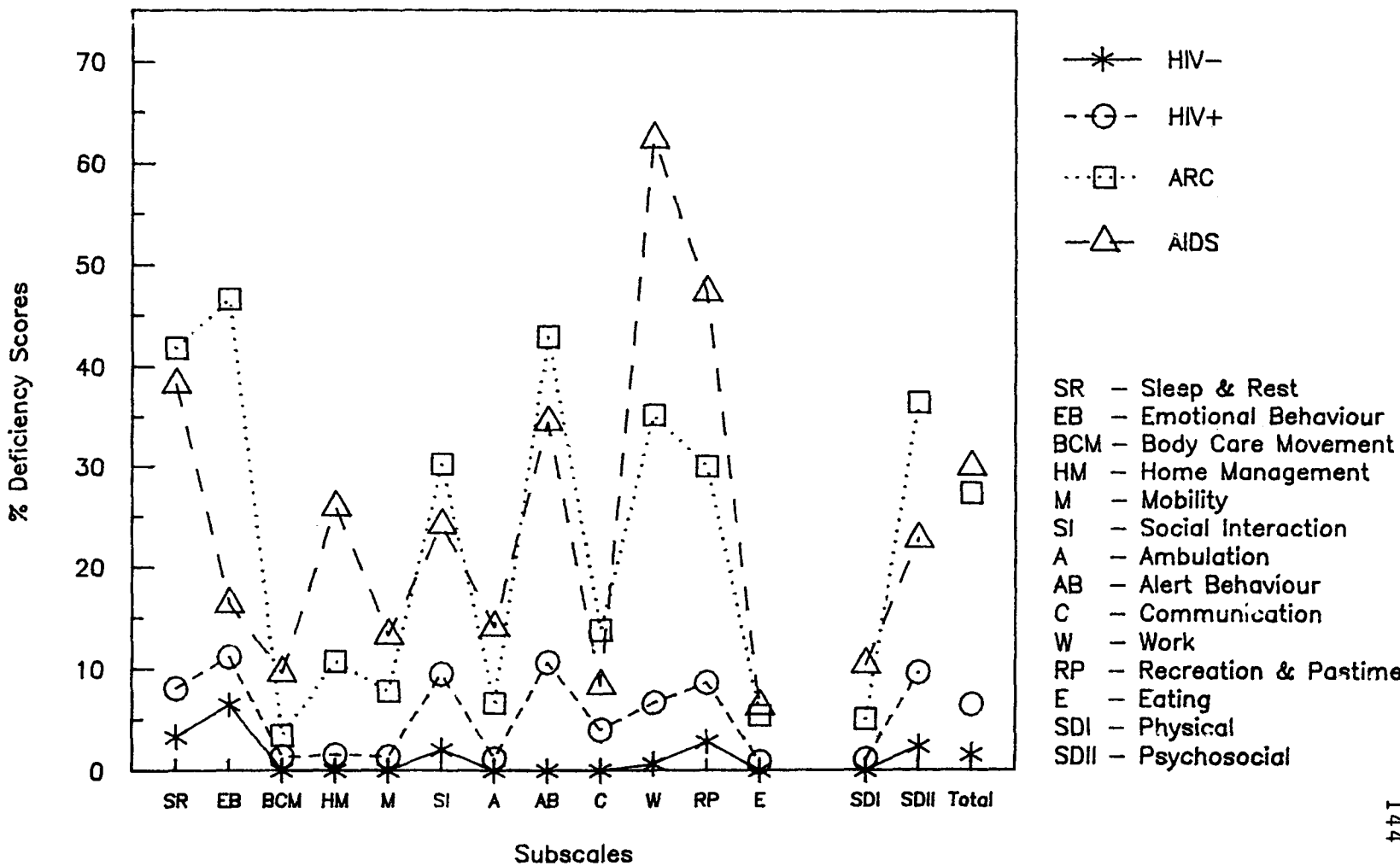


Table 6.45

Statistical Analysis of Hypothesis 5:
MMPI Data of the AIDS Group
Versus all Other Groups

(N = 59)

HYPOTHESIS 5: AIDS vs HIV- HIV+, ARC

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.56652	3.51980	10.00	46.00	.002

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Hypochondriasis	21.09087	.000	HIV-,HIV+ < ARC,AIDS
Depression	3.58753	.063	---
Hysteria	13.17107	.001	HIV-,HIV+ < ARC,AIDS
Psychopathic Deviate	0.04980	.824	---
Masculinity-Femininity	0.81789	.370	---
Paranoia	1.35445	.250	---
Psychasthenia	0.25302	.617	---
Schizophrenia	3.51618	.066	---
Hypomania	2.75760	.102	---
Social Introversion	0.54955	.462	---

Table 6.46

**Statistical Analysis of Hypothesis 5:
SIP Data of the AIDS Group Versus
All Other Groups**

(N = 59)

HYPOTHESIS 5: AIDS vs HIV-, HIV+, ARC

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.14543	21.54515	12.00	44.00	.000

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Sleep & Rest	13.51898	.001	HIV-,HIV+ < ARC,AIDS
Emotional Behaviour	0.71559	.401	---
Body Care & Movement	27.93260	.000	HIV-,HIV+,ARC < AIDS
Home Management	38.28968	.000	HIV-,HIV+,ARC < AIDS
Mobility	15.84614	.000	HIV-,HIV+ < AIDS
Social Interaction	7.20731	.010	HIV-,HIV+ < ARC,AIDS
Ambulation	36.81499	.000	HIV-,HIV+,ARC < AIDS HIV- < ARC
Alert Behaviour	5.04720	.029	HIV-,HIV+ < ARC HIV- < AIDS
Communication	0.55257	.460	---
Work	91.27303	.000	HIV-,HIV+,ARC < AIDS HIV-,HIV+ < ARC
Recreation & Pastimes	39.66099	.000	HIV-,HIV+ < ARC,AIDS
Eating	12.82722	.001	HIV-,HIV+ < ARC,AIDS

primarily. However, on both these scales, pairwise comparisons using Tukey's HSD demonstrated that the AIDS patient group obtained higher scores than the healthy groups (HIV- & HIV+), but not significantly so when compared to the ARC patients. Univariate F tests performed on the SIP subscales revealed that the significant group effect derived from all subscales, with the exception of Emotional Behaviour and Communication. Post hoc analyses confirmed that the AIDS group achieved significantly greater scores than the remaining three groups on Body Care & Movement, Home Management, Ambulation, and Work. However, the AIDS group was significantly different from both healthy groups (HIV- & HIV+), for Sleep & Rest, Mobility, Social Interaction, Recreation & Pastimes, and Eating. A group effect on Alert Behaviour was observed between AIDS and HIV- only.

HYPOTHESIS 6: The ARC group will disclose greater anxiety levels than the AIDS group.

The outcome of this analysis is presented in Table 6.47. The multivariate F test corroborated the group effect overall, while the univariate F tests indicated significance for both State and Trait measures. Mean scores were in the predicted direction, that is ARC patients were more anxious than AIDS patients. Figure 6.5 provides a dramatic representation of the difference in anxiety levels in the

Table 6.47

Statistical Analysis of Hypothesis 6:
STAI Data of the ARC Group Versus the AIDS Group

(N = 28)

HYPOTHESIS 6: ARC vs AIDS

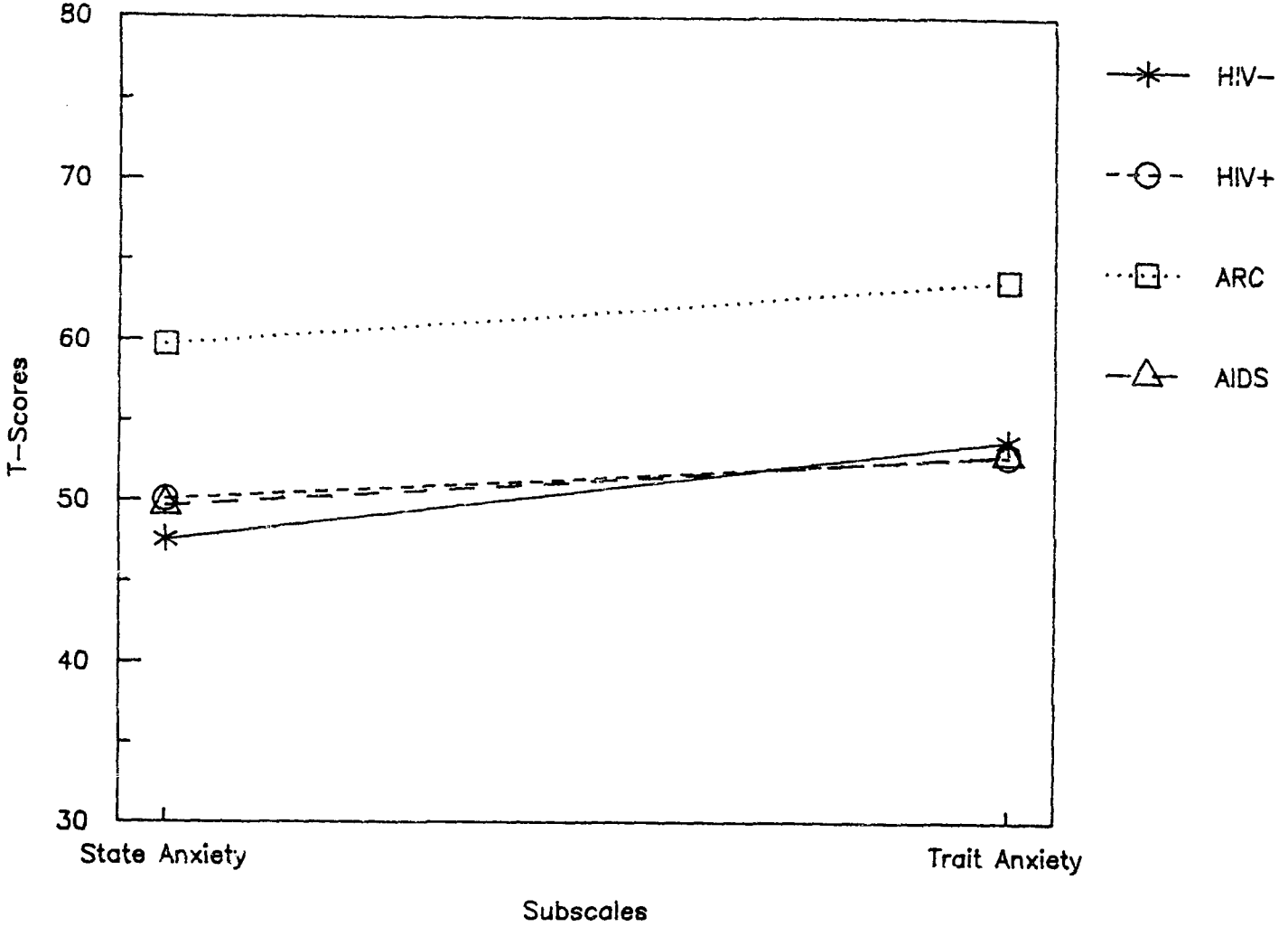
Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.83874	5.19106	2.00	54.00	.009

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
State Anxiety	7.89707	.007	HIV-,HIV+,AIDS < ARC
Trait Anxiety	8.42610	.005	HIV-,HIV+,AIDS < ARC

Figure 6.5
STAI Mean Scores of Medical Diagnostic Groups



ARC group in comparison to all other medical diagnostic categories.

HYPOTHESIS 7: When compared to the healthy groups (HIV- & HIV+), ARC patients will exhibit a greater pattern of emotional dysfunction overall (MMPI, SIP, and STAI).

Tables 6.48, 6.49 and 6.50 contain the analyses supporting the hypothesis that the ARC group is significantly different from the HIV- and HIV+ groups on the MMPI, the SIP, and the STAI, respectively. Univariate F tests of the MMPI indicated that Hypochondriasis, Depression, Hysteria, Psychasthenia, Schizophrenia, and Social Introversion contributed to the group effect. Post hoc analyses were consistent with these findings on the Hypochondriasis, Depression, Hysteria, and Psychasthenia scales.

All but one subscale (Body Care & Movement) of the SIP test demonstrated the univariate group effect. Pairwise comparisons reported the difference between ARC and healthy groups (HIV- & HIV+) on Sleep & Rest, Emotional Behaviour, Social Introversion, Alert Behaviour, Work, Recreation & Pastimes, and Eating. Differences between the ARC and HIV- groups were reached for Ambulation and Communication.

Finally, the univariate F tests and the post hoc analyses conducted on the STAI subscales both susbstantiated hypothesis 7, for State and Trait measures.

Table 6.48

Statistical Analysis of Hypothesis 7: MMPI Data of the ARC Group Versus both Healthy Groups

(N = 45)

HYPOTHESIS 7: ARC vs HIV-, HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.54345	3.86451	10.00	46.00	.001

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Hypochondriasis	21.34188	.000	HIV-,HIV+ < ARC,AIDS
Depression	11.14421	.002	HIV-,HIV+ < ARC
Hysteria	16.49107	.000	HIV-,HIV+ < ARC,AIDS
Psychopathic Deviate	2.32403	.133	---
Masculinity-Femininity	0.13006	.720	---
Paranoia	2.89073	.095	---
Psychasthenia	12.90600	.001	HIV-,HIV+ < ARC
Schizophrenia	7.34831	.009	---
Hypomania	1.25687	.267	---
Social Introversion	6.46477	.014	---

Table 6.49

Statistical Analysis of Hypothesis 7: SIP Data of the ARC Group Versus both Healthy Groups

(N = 45)

HYPOTHESIS 7: ARC vs HIV-, HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.39801	5.54592	12.00	44.00	.000

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
Sleep & Rest	37.83639	.000	HIV-,HIV+ < ARC,AIDS
Emotional Behaviour	39.20201	.000	HIV-,HIV+,AIDS < ARC
Body Care & Movement	3.08813	.084	---
Home Management	7.24744	.009	HIV-,HIV+,ARC < AIDS
Mobility	7.07496	.010	HIV-,HIV+ < AIDS
Social Interaction	36.61106	.000	HIV-,HIV+ < ARC,AIDS
Ambulation	9.37141	.003	HIV-,HIV+,ARC < AIDS
			HIV- < ARC
Alert Behaviour	23.06721	.000	HIV-,HIV+ < ARC
			HIV- < AIDS
Communication	10.69294	.002	HIV- < ARC
Work	35.57468	.000	HIV-,HIV+,ARC < AIDS
			HIV-,HIV+ < ARC
Recreation & Pastimes	19.06307	.000	HIV-,HIV+ < ARC,AIDS
Eating	16.22916	.000	HIV-,HIV+ < ARC,AIDS

Table 6.50

Statistical Analysis of Hypothesis 7: STAI Data of the ARC Group Versus both Healthy Groups

(N = 45)

HYPOTHESIS 7: ARC vs HIV-, HIV+

Multivariate F Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.78140	7.55329	2.00	54.00	.001

Univariate F Tests with (1, 55) degrees of freedom

Variables	F Value	Sig. of F	Tukey's HSD
State Anxiety	12.99010	.001	HIV-,HIV+,AIDS < ARC
Trait Anxiety	10.63526	.002	HIV-,HIV+,AIDS < ARC

Relationships between data sets

The potential impact of the emotional and affective state on the neurocognitive functions was explored. To this end, a canonical correlation was conducted between the psychological and neuropsychological data sets. In view of the relatively low subject-to-variable ratio, the results of this analysis will be used to generate hypotheses and would require further replication. The analysis was based on the unique factors underlying each data set primarily. The first data set included the 6 factors extracted from the neuropsychological test battery, while the second data set was comprised of 3 factors derived from the MMPI, 2 from the SIP, and both mean scores from the STAI. Table 6.51 summarizes the results of the canonical correlation between the two data sets.

A canonical correlation constitutes the highest degree of interrelationship between two linear combinations of variables. The linear combinations of variables from each data set constitute the canonical variates. The procedure yielded one meaningful canonical correlation ($p = 0.003$), implying that there is only one unique dimension of common variance between the two domains. The square of the canonical correlation represents an estimate of the variance shared by the two canonical variates. The current results indicate that 38% of the variance is shared by the two

Table 6.51

Canonical Correlation: Relationship Between the Neuropsychological and Psychological Data Sets

(N = 59)

Multivariate F-Test

Test Name	Value	Exact F	Hypoth. DF	Error DF	Sig. of F
Wilks	.24374	1.83283	42.00	219.21	.003

Root No.	Eigenvalue	Canonical Correlation	% Variance
1	0.60962	0.61542	0.37874
2	0.38728	0.52836	0.27917
3	0.31992	0.49232	0.24238
4	0.23836	0.43873	0.19248
5	0.12192	0.32966	0.10867
6	0.00190	0.04352	0.00189

Loadings of the canonical variate of the Neuropsychological Data

Variable	Canonical Variate 1
Neuropsy. Factor 1	.36722
Neuropsy. Factor 2	.07760
Neuropsy. Factor 3	.82439
Neuropsy. Factor 4	-.12207
Neuropsy. Factor 5	.40217
Neuropsy. Factor 6	.05358

Loadings of the canonical variate of the Psychological Data

Variable	Canonical Variate 1
MMPI Factor 1	-.80644
MMPI Factor 2	.12139
MMPI Factor 3	-.28095
SIP Factor 1	-.80470
SIP Factor 2	-.46232
STAI State	-.14910
STAI Trait	-.38118

canonical variates, reflecting only a modest association between the two data sets.

The correlations of the variables with the canonical variates reflect the structure of the variates. As a rule of thumb, a structure coefficient >.30 is considered meaningful (Pedhazur, 1982). Using this criterion, factors 1, 3, and 5 constitute the most critical neuropsychological dimensions associated with the canonical variate. In the psychological data set, the first MMPI-factor and both SIP-factors contribute the most to the linear combination. Stated differently, the structure coefficients suggest that the association between the two sets of data is determined on the one hand by rate of information processing, verbal/language skills, motor strength, and motor speed, and by emotional reactions, physical limitations, and psychosocial aspects on the other.

Furthermore, it is possible to determine the proportion of the total variance of each battery that can be accounted for by the canonical variates (see Pedhazur, 1982, for the procedure to follow). In the neuropsychological test battery, the canonical variate accounts for 16.7% of the total variance of the six factor-variables. In the psychological data set, the canonical variate reflects 25.3% of the variance.

Finally, the redundancy coefficients form a second set of structure correlations indicating which variables in one

battery are associated with (accounted for, or explained by) the variates from the other battery. (See Pedhazur, 1982 for procedure). In the current analysis, the predictable variance of the neuropsychological factor scores from the linear combination of the psychological data is only 6.3%, while the predictable variance of the psychological data from the linear combination of the neuropsychological tests is merely 9.6%.

CHAPTER SEVEN

DISCUSSION OF RESULTS

Epidemiological Data

The demographic characteristics of the volunteers recruited for this study are compatible with those described in the literature (CDC, 1982a & 1982f; Gottlieb, Schroff, Schanker, et al., 1981; Masur, et al., 1981). Hence, the participants constituted a representative sample of the homosexual population which has been identified as a group at increased risk of being infected by HIV and contracting AIDS. The homosexual population is found to be at particular risk in view of its "fast lane lifestyle" (Jaffe, Choi, Thomas, et al., 1983; Marmor, 1984). More specifically, these are primarily men in their thirties, who typically have consumed recreational and inhalant drugs, and bear frequent histories of sexually transmitted diseases. Although the issue of multiple sexual partners was not investigated systematically, information regarding a high frequency of promiscuity often transpired during the personal interview with the volunteers. In contrast, the seronegative group tended to be more monogamous, and/or to have been involved with a limited number of sexual partners only.

The results concerning the pattern of recreational drug ingestion are of particular interest. The percentage (86 to

93%) of the HIV infected participants who have made use of recreational drugs on a more frequent basis or via an habitual pattern differs notably from that of the seronegative group (53%). A similar pattern of distribution was found with respect to the use of hallucinogens (35% versus 79 to 86%). As certain recreational and inhalant drugs can induce transient immunosuppression (Council on Scientific Affairs [CSA], 1984; Macek, 1982), it has been suggested that these may contribute to render the organism more susceptible to contract HIV infection, and may function as co-factors in the development or course of the disease (CSA, 1984). The findings depicted here are thus consistent with the published observations.

The possible interactions between substance abuse and neuropsychological findings were not analyzed specifically in this study. In light of the distribution described above and the absence of significant differences between HIV- and HIV+ on neurocognitive tests and psychological measures, it would appear that use of recreational drugs had little effect on profile scores achieved. This issue was examined explicitly by San Giovanni and his colleagues (1989) in patients with diagnosed AIDS. Their results indicated that mild to moderate substance use did not exacerbate the notable neuropsychological deficits observed in their sample (San Giovanni, Boccellari, Dilley, & Davis, 1989).

There have been reports of an inflated incidence of autoimmune disorders in left-handed individuals (Geschwind & Behan, 1982). In the present series of participants, cerebral dominance was established by documenting the preferred hand for writing, and a lateral preference examination for eye, hand, and foot. Geschwind and Galaburda (1985a; 1985b; 1985c) suggested the presence of a T-cell dysregulation in individuals displaying anomalous dominance (i.e. sinistrality). This implies that individuals with a strong left-handed preference (i.e. right hemisphere dominance) would be more susceptible to HIV infection and its complications. In this study, the statistical analyses failed to support an asymmetrical distribution of sinistrality in the nonhealthy groups, although the only three left-handed participants were in fact affiliated with the ARC and AIDS patient groups. Fernandez and his colleagues reported a disproportionate representation of left-handedness in their small (n=19) study group of ARC patients, with 68% dextrals and 32% sinistrals (Fernandez, Adams, Levy, et al., 1988). However, no association was found between handedness and risk of HIV infection or progression of illness in large samples of homo/bisexual men such as in the Multicenter AIDS Cohort Study (MACS) group. The distribution of hand preference in 881 HIV- individuals was 57% right-handed, 6% left-handed, and 37% ambidextrous; the 723 HIV+ group followed a similar

pattern with 60% dextrals, 7% sinistrals, and 33% ambidextrals (Becker, Kingsley, Bass et al., 1989).

Not surprisingly, the healthy groups deviated from the nonhealthy ones with respect to occupational status, use of alcohol at the time of assessment, and the presence of CNS-related symptoms. ARC and AIDS patients were often unable to resume regular work in view of the recurrent systemic illnesses they suffer, and occasionally because of the social stigma associated with their affliction. Consumption of alcohol is often contraindicated in combination with the therapeutic management prescribed. It was noted that AIDS and ARC patients have a higher tendency to adopt a more "healthy" lifestyle following recognition of HIV infection. Several individuals spontaneously reported changing their diet, supplementing it with vitamins, exercising regularly, and practicing relaxing activies such as meditation and Tai Chi. Similarly, a small percentage (14%) of the HIV+ individuals abstained from drinking alcohol and changed their life habits, in order to assure a healthy and competent immune system.

Headaches were more frequently reported by the unhealthy groups, particularly by the ARC patients. The finding, taken in concert with the fact that the ARC group also displayed higher levels of anxiety, may reflect a greater frequency of tension headache in this population.

Given the uncertainty of their future, it is not unusual for them to complain of psychological distress.

On the other hand, complaints of headaches have also been observed as an early sign of HIV brain infection (Navia, et al., 1986b). In the face of apparently preserved neuropsychological functioning, neurologic symptoms may appear transiently at the time of seroconversion. Marder and her colleagues uncovered comparable prevalence of overt non-cognitive neurological signs in HIV+ and HIV- men (Marder, et al., 1989). They reported that although HIV+ men were more likely to complain of compromised concentration and memory functions, they were nevertheless similar to the HIV- group with respect to the presence of cranial nerve abnormalities, pyramidal and extrapyramidal features, frontal release signs, peripheral neuropathy, and impairments on a short mental status exam. Subjective neurological complaints were reported in 84% of HIV+ and 74% of HIV- men, a distribution which was not found to be statistically different (Collier, et al., 1989). The relatively high number of headache complaints observed in the current study is thus compatible with published findings from other investigatory groups.

Neuropsychological Data

Participants who are experiencing clinical manifestations of HIV infection and meet the criteria for

the nonhealthy groups definitely achieved lower scores than members of the healthy groups. Consistent with previous reports (Meer, 1986; Navia et al., 1986b), measures of cognitive abilities, psychomotor speed, mental flexibility, and motor functions emerged as critical indices of cerebral involvement between the two health status groups. The first hypothesis was thus confirmed and the present results replicate the findings from several other research groups (e.g. Grant et al., 1987; Kobayashi, Heaton, Thompson, et al., 1989; Martin et al., 1989a, 1989c, 1989d; Miller et al., 1989a, 1989b; Parisi, Strosselli, Barbarini, et al., 1989; Tross et al., 1988).

The relatively consistent linear trend between the four medical diagnostic groups constitute the most striking aspect of the neuropsychological test results obtained. For the most part, the seronegative group displayed the best mean scores, followed next by the healthy seropositive group, the ARC group, and with the AIDS group faring worst. The diminished performance level observed in the AIDS group becomes most apparent when specific underlying abilities (factor scores) are evaluated in contrast to a wide spectrum of brain functions (whole test battery). Such a finding suggests that the brain is not compromised diffusely but that particular areas of functioning are involved. The most prominent features noted in this study included speed of information processing and execution, visual memory and

learning, measures of verbal intelligence and naming, as well as motor speed and strength.

The diagnostic distinction that exists between the AIDS and the ARC syndromes is interpreted as a continuum of immune dysregulation. This clinical differentiation does not appear to hold true with respect to the functional status of the brain where HIV infection is concerned. Namely, dementia has also been identified as the first or the only predominant manifestation of HIV infection (Abos et al., 1989; Galgani et al., 1989; Navia & Price, 1987; Wilson et al., 1989b). Some of these cases actually die before they develop the full blown spectrum of immune suppression and AIDS.

The current data also reflect the fact that AIDS and ARC patients display comparable performance levels on the neuropsychologic tests. This finding may shed some light as to why the AIDS patients were only mildly different from the remaining three groups on the total test battery (Hypothesis 2). Although the AIDS group did display the poorest cognitive profile of all, the lower mean scores of the ARC group contributed to reduced mean difference scores between AIDS and the three other groups. As mentioned earlier, the distinction becomes most apparent when asymptomatic individuals were contrasted to symptomatic ones (Hypothesis 1). Whether there is a greater percentage of AIDS patients that succumb to an HIV-related encephalopathy remains to be

determined. The presence of lower mean scores in the ARC group would thus contraindicate the combination of these patients with the healthy groups when comparing performance levels with the AIDS groups. Consequently, future studies investigating neuropsychologic dysfunction would be best served if AIDS and ARC patients were considered together as a group. This observation is in keeping with the new CDC classification system for HIV infection, whereby the ARC patients are part of Group IV together with all other AIDS defining illnesses. Contemporary studies typically compare the performance rate of a) seronegative controls to aysmptomatic HIV+ (CDC II) and/or LAS syndromes (CDC III); and b) symptomatic HIV+ (CDC IV) to seronegative controls and to CDC II/III individuals.

In light of the homogeneity of the participant pool with respect to attribute variables and epidemiological characteristics, the present data intimate that the AIDS and ARC patient groups are experiencing some degree of functional change, albeit mild in nature, despite the fact that they are not displaying overt signs of dementia or neurological symptoms at the time of their evaluation. Thus, the current findings further substantiate the postulate that there may be a latent subclinical infection, whereby HIV affects the brain even before manifest symptoms actually progress to an acute encephalitis or a full blown AIDS dementia-complex. Most important however is the fact

that all mean scores still fall within normal limits from a clinical perspective.

The lack of distinction between the ARC group and the two healthy ones had been predicted in view of the all inclusive nature of the ARC diagnostic category at the time of this investigation. The constitutional signs and symptoms which accompany the lymphadenopathy syndrome are quite diverse and result in different degrees of illness, discomfort, and asthenia. Hence, it was thought that there would be much variability in performance within this group, and that only the more exacting tasks would prove to be affected more consistently. Based on clinical judgement, it was felt that the Consonant Trigrams and the PASAT tests (Hypothesis 3) would contribute to differentiate the ARC group from healthy individuals, as both of these tasks require sustained attention and dual conceptual tracking simultaneously.

The hypothesis was confirmed only partially, i.e. for the Consonant Trigrams but not for the PASAT. The discrepancy for the sensitivity of these two measures is interpreted in the following light. On the Consonant Trigrams task, the examinee is also being evaluated for his ability to perform in the presence of interference material, whereas this component is not present in the PASAT. In the latter, speed of information processing constitute the more relevant feature. Thus, it appears that interference

conditions are more taxing than a limited time for response latency. To the best of my knowledge, the Consonant Trigrams test has not been used systematically by other research groups. Further studies are thus necessary to replicate the current results.

However, a significant difference was noted between the ARC and both healthy groups on a measure of fine motor speed. The finding was further substantiated when the specific underlying dimensions (factor scores) were examined. This observation is in keeping with previously published reports of motor dysfunction as an early sign of HIV brain involvement (Jordan, et al., 1985),

As expected, the overall neuropsychological profile of the healthy seropositive group was comparable to the one of the seronegative group. The absence of clinical manifestations and cerebral involvement would appear to indicate that these individuals continue to be asymptomatic carriers. Before the neurological complications of HIV infection were fully recognized, the World Health Organization (1985) reported the incubation period for immune dysregulation to occur between 6 months and 5 years. As for AIDS encephalopathy, the period during which the HIV remains latent is still unknown, and needs to be systematically investigated. Attention has been given primarily to the incidence, prevalence, clinical expression, and pathological correlates of the CNS involvement. More

recent studies attempt to identify immunological parameters which could be used as predictors of neuropsychological dysfunction. The results of these preliminary findings will be reviewed in the following chapter.

The neuropsychological test battery administered in this exploratory study was exhaustive and probably unduly time-consuming to be considered useful and/or cost effective in a clinical setting. The results of the various analyses conducted in this research were examined in order to distinguish which measures prove to be most sensitive in detecting neuropsychological dysfunction associated with HIV infection. The following discussion is thus based on the outcomes of the principal component analysis, findings from the specific a priori hypotheses and the exploratory analyses by functional areas, as well as those from the global judgement of neuropsychologic impairment.

Most consistently, measures which reflected the rate of cognitive processing appeared critical in illustrating changes in performance level. Time of execution featured as the first underlying dimension of this battery of tests. Examination of mean scores suggests that time increases with the diagnostic categories indicating a decline of efficiency as the diseases progresses. The pattern was observed even in relatively simple tasks of identification (e.g. Visual Search) and recognition (e.g. Tactile Form Perception).

Measures which take into account higher executive functions such as sustained and divided attention, mental flexibility, and/or dual conceptual tracking within a time frame (e.g. Trail Making Test, PASAT) also appear to be most sensitive to cerebral dysfunction. In particular, the decreased performance noted on the Trail Making test has also been reported by other researchers (Grant et al., 1987; Kobayashi et al., 1989; Miller et al., 1989a, 1989b; Van Gorp et al., 1989b; Wilson et al., 1989b). In contrast, group mean scores from the PASAT were not as contributory as expected. The apparent discrepancy between the present results and those of Grant et al. (1987) on the PASAT stem from two sources. Firstly, the two AIDS group appear different. While all three other groups achieved similar results, the AIDS mean accuracy scores in the current sample (n = 14) revealed better performance (ranging from 37.0 $\pm$ 7.5 to 23.4 $\pm$ 4.7 on the first to the last speed) than in their sample (n = 15, 28.0 $\pm$ 10.1 to 14.4 $\pm$ 9.6). Secondly, the discrepancy in findings may also derive from the interpretation of dissimilar scores. Grant and his colleagues analysed and reported the scores obtained on the first and slowest speed only, whereas the current results included all four speed trials. As a person is exposed to the task repeatedly, there is often an improvement in performance as one may become more comfortable and learn to adopt coping strategies to deal more effectively with the

requirements at hand. In the current sample, probable impairments (using criteria from Grant et al. 1987) were noted in 59% of the participants when performance of the first speed trial only is evaluated. In contrast, probable and/or definite impairments based on the total scores reached only 29%.

All measures involving time scores seem to be particularly sensitive in comparison to accuracy and content data. This finding has been observed in several other research groups who have consequently incorporated simple and/or choice reaction time tests to their battery as measures of decision processing time (e.g. Martin, et al., 1989c, 1989d; Miller, et al., 1989a; Stern, Sarno, Williams, & Gorman, 1989). In comparison to HIV- individuals with adjustment disorders, relatively asymptomatic HIV+ individuals displayed reduced cognitive processing speed which could not be explained by constitutional symptoms, anxiety and/or depression (Martin, et al. 1989a). It was concluded that the slowed mentation may represent early signs of ADC and is suggestive of basal ganglia and nigrostriatal system involvement.

With respect to memory and learning measures, probable and definite impairments were observed more consistently with tests of visual learning and visual memory (e.g. Rey-Osterrieth Complex Figure & Rey Nonverbal Learning Test) than with tests using verbal material. Less than optimum

performance on nonverbal memory tasks has been reported most consistently (Claypoole et al. (1989); Kobayashi et al., 1989; Saykin, Sprehn, Janssen, et al., 1987; Van Gorp et al., 1989a). With respect to manipulation of verbal information, examination of verbal learning scores indicated comparatively greater difficulty than recall of logical passages. In this investigation, the delayed recall time period extended to 30 minutes for all tasks, and statistical significance was reached in all but one univariate comparisons of Healthy versus Nonhealthy groups on the memory/learning tests used. Grant and his collaborators (1987) used a one hour delay and failed to obtain statistical significance on their long-term memory trials. Verbal memory deficits have nevertheless been reported inother studies (Kobayashi et al., 1989; Levy, Fernandez, Holmes, et al., 1987; Saykin, et al., 1987 & 1988; Stern et al., 1989a, 1989b). Verbal short-term memory and learning decreases with the severity of ADC (Dorfman, Keilp, Sadler, et al., 1989). Finally, the current results also revealed a susceptibility to lose information in the face interference material (Consonant Trigrams) which has not been reported previously and requires replication.

Motor functions were typically affected in the nonhealthy groups. Both grip strength and speed of fine motor movement repeatedly emerged as discriminating measures. Various measures of reduced motor speed have been

documented in the literature (Saykin, et al., 1987; Van Gorp, et al., 1989a, 1989b; Wilson, Thompson, & Riccio, 1989). Selnes and colleagues have criticized the use of motor tasks in studies using brief screening batteries (Selnes et al., 1989). They belabored the fact that motor slowing may be secondary to peripheral neuropathy and constitutional physical weakness, and not necessarily associated with subcortical dysfunction.

From the series of verbal cognition and language tests, group differences were noted for the Verbal IQ, with probable and definite impairments occuring primarily on the Digit Span subtest. This finding is consistent with those of Grant et al. (1987), and suggests that the auditory attention span may be compromised. Various aspects of language functions have typically not been compromised. Kobayashi and his colleagues (1989) found no significant differences between AIDS patients and seronegative controls on auditory and reading comprehension, verbal fluency, naming, repetition and articulation. However, discrepant findings have been reported with respect to word fluency by Saykin, Janssen, Sprehn, et al. (1988), Stern et al. (1989), and Wilson et al. (1989). This ability did emerge as a meaningful structure in the fourth factor of the current battery of test. Since overall language functions are not typically compromised, and that verbal fluency loaded significantly with Consonant Trigrams, the following

interpretation may shed some light. Both measures involve retrieval of information, and both must do so in the presence of interference material. In the Word Fluency task, the individual must access target words from the lexicon and inhibit the production of unacceptable words (e.g. those beginning with a capital, verbs with a different conjugation, perseverations). In the Consonant Trigram, the individual must retain three letters while he is requested to execute a mental control task thereby prohibiting the rehearsal of information in the working memory store. Thus an increased susceptibility to interference material may be the key factor. Additional investigations are required to verify this hypothesis.

The Performance IQ was found to be significantly different only in one comparison and the Digit Symbol subtest suggested probable and definite impairments in a small number of participants (15%). Psychomotor speed is particularly important in this task. Occasional dysfunction was also observed on Object Assembly and Block Design which involve **rapid** part-to-whole integration and visual-spatial skills. The remaining two nonverbal measures (Picture Completion and Picture Arrangement) were not particularly sensitive overall, and also did not involve a time component as much.

Selnes and his collaborators have recently argued that the WAIS-R may not be the most appropriate test of

intelligence and cognition to be used in this population. Deficits were frequently observed on Digit Span and the time components of the Performance subtests (Selnes, et al. 1989). They recommended that the vocabulary and abstraction subtests of the Shipley Institute of Living Scale be used as a more representative index of the intellectual potential, and that they may be more resistant to the effects of HIV infection.

Finally, based on the current sample study, the cognitive functions which seem to have remained relatively intact and show most resistance to early detection of CNS-related HIV infection include the following: auditory comprehension, constructional praxis, visuospatial organization, right-left orientation, face recognition, and finger localization.

On the whole, the findings observed in this study are consistent with a subcortical form of dementia where the cardinal symptoms feature slowing of mental processes, forgetfulness, and reduced efficency in manipulating acquired knowledge. The presenting picture contrasts well with the cortical dementias where aphasia, amnesia, and agnosia constitute the primary hallmarks (Cummings & Benson, 1984).

Personality and Emotional Aspects

The consistent linear trend which was seen in the neuropsychological profiles is not present in the personality data; the gradual decrease in function from HIV- to AIDS is no longer apparent. Rather, the pattern of results from the psychological data attest to a more abrupt change between the Healthy and Nonhealthy individuals. In particular, there appears to be a greater amount of dysfunction in the ARC group: several subscales of the MMPI and the SIP, composite scores of the SIP, and both anxiety scores of the STAI are most elevated in the ARC group, followed closely by the AIDS group. An a priori hypothesis (# 6) for this direction had been predicted for the STAI scales only. Scales pertaining more directly to physical constitutional symptoms and daily activities were more elevated in the AIDS than the ARC group. Both healthy groups show a much lower profile.

MMPI. This personality inventory consists of four validity and ten clinical scales. Examination of the validity scales indicated that all protocols were valid and interpretable. The prominence of the Masculinity-Femininity scale reflecting interests more compatible with a feminine orientation across all participants was noteworthy. The clinical interpretation of this elevation confirms the sexual orientation of the study sample, and the homogeneity of the participant pool.

On the whole, Nonhealthy individuals show significantly more evidence of elevated emotional distress (Hypothesis 4) in comparison to the Healthy participants. The profiles plotted in Figure 6.1 (p. 131) depict the areas of differentiation. The Healthy group displays a profile within the normal range; none of the scales suggest areas of psychopathology. In contrast, the Nonhealthy group exhibits several areas of dysfunction. The most prominent aspects of the profile are concerns over bodily functions, physical discomfort, and the experience of pain, fatigue and/or weakness. Not surprising are concomitant feelings of dysphoria or sadness, rumination, and loss of initiative. Participants in this group also appear to be experiencing some degree of turmoil or distress which may lead to impaired abilities in concentration, judgement, and thoughts. Reports of agitation, tension, nervousness, and preoccupation are also present to some extent.

Profiles of the four medical diagnostic groups (Figure 6.3, p. 143) illustrate the absence of psychological dysfunction in both healthy HIV- and HIV+ groups. In contrast, elevated scores were observed in ARC and AIDS groups who display a parallel configuration overall.

The MMPI has not been used extensively in AIDS research. In one report however, a shorter version of this test (MMPI-168) was administered (Saykin, Jansen, Sprehn, et al., 1989). As in the present study, Saykin and associates

(1989) found that the ARC group displayed greater amount of somatic complaints, dysphoric mood, anxiety, and social isolation than seronegative controls, while asymptomatic HIV+ and LAS groups did not differ from the seronegative controls.

Individuals at risk of contracting HIV may endure several depressive experiences in light of the progression of the disease, the loneliness and social isolation, the loss of loved ones to AIDS, dissatisfaction with social support, and availability of support persons (Castro, Coates & Ekstrand, 1989). Contrary to expectations, an exploration of the psychiatric overlay of numerous AIDS deaths and of other major negative life events revealed a lack of direct association between an increased number of losses and any depressive scores such as those produced by the Beck Depression Inventory, the Hamilton Depression Scale, the Dohrenwend Demoralization Scale, and the Symptoms Check List-53 (Neugebauer, Williams, Rabkin, et al. 1989). The pattern of these paradoxical results proved to be the same for both HIV seronegative and seropositive individuals. The authors felt that these findings did not reflect denial and/or indifference. Instead, they entertained several interpretations to account for this lack of association between AIDS death and depression: i) a possible alteration in the perception of loss and death, ii) a capacity for adaptive habituation, iii) defiance, and iv) poor social

integration, isolation, and depression preceding the AIDS epidemic. In contrast to the above findings, other studies have produced results indicating more dysphoric mood in the seropositives (CDC II/III) than in the seronegatives (e.g. Herns, et al., 1989). In particular, anxiety and/or depression appear to rise markedly at the time of HIV-status diagnosis (Jadresic, Riccio, Hawkins, et al., 1989). However, the examination of coping style has revealed that during the course of time, the wariness and disturbing effects of HIV-diagnosis dissipate, and the psychological distress abate (Leiberich, Engeter, Hermann, et al., 1989). All seropositive participants in this study were several months post diagnosis and may have suffered a more acute and reactive episode of anxiety and depression at such time. The elevations depicted on the profile are not extreme and suggest a tendency for impoverished morale, decreased involvement and/or poor motivation, and not of a severe clinical depression.

SIP. This questionnaire evaluates twelve areas of functioning and provides supplementary indices of physical, psychosocial, and global functioning. Healthy individuals are expected to obtain subscale and composite scale scores of 0%. For the purpose of this study, scores exceeding 5% are considered indicative of notable dysfunction.

As shown in Table 6.29 (p. 121), all subscale and composite scores of the Nonhealthy group surpass 5%, confirming significant problems in performing basic life activities and aspects of psychosocial involvement. Major areas of difficulty include Work (49%)[1], Sleep & Rest (40%)[1], Recreation & Pastime (39%)[1], Alert Behaviour (39%)[1], Emotional Behaviour (31%)[1], Social Interaction (27%)[1], and Home Management (18%)[1]. In the Healthy group, only one subscale score (Emotional Behaviour) is indicative of impairment (9%)[1], while three scores border the cut-off point (Recreation & Pastime, Sleep & Rest, and Social Interaction).

As expected, formal analyses reveal that all subscale and composite scores of the SIP differentiate the areas of dysfunction between Healthy and Nonhealthy groups (Hypothesis 4). Similarly, when the AIDS group is compared to the other three medical categories (Hypothesis 5), it achieves significantly greater SIP scores on the whole. However, only one third of the subscales demonstrate statistically higher dysfunction levels than those of the three other groups: they consist of Work, Home Management, Ambulation, and Body Care & Movement. Also congruent with these findings is the larger score obtained on the physical composite dimension.

[1] Note: Number in parentheses indicate degree of dysfunction

Supplementary analyses also disclose that the AIDS group displays higher elevations on the SIP overall than the ARC group. More specifically, areas such as Work, Recreation & Pastime, Home Management, Ambulation, and Body Care & Movement are particularly more impaired in the AIDS group than the ARC. In contrast, the ARC group seems to experience more difficulties than the AIDS group in five functional areas: Emotional Behaviour, Alert Behaviour, Social Interaction, Communication, and Sleep & Rest. The first four of these constitute the Psychosocial index, which is also higher in the ARC group. However, only Emotional Behaviour reached statistical significance. Here again, larger sample sizes may be essential to uncover significant differences between ARC and AIDS patients. As seen in the MMPI, HIV- and HIV+ groups obtained similar SIP scores and are not significantly different from each other.

The pattern of results from the SIP suggests a dissociation with respect to the types of dysfunctional areas between AIDS and ARC groups. Although both physical and psychosocial functions are impaired, physical and basic life activities appear to predominate in the AIDS group, whereas emotional and social disturbances seem to be more pervasive in the ARC group.

STAI. Two measures of anxiety are available from this test: one which assesses anxiety level specifically at the time of administration (state), and one which is more

representative of the individual's usual condition (trait). In contrast to the MMPI and SIP measures, there is only a tendency for Healthy and Nonhealthy groups to be different from each other on this test. As predicted, the ARC group achieves the highest ratings of all, reporting significantly higher anxiety levels than the AIDS and the Healthy groups on both scales. No differences were noted between HIV- and HIV+ individuals on both scales. State and Trait anxiety scores of the AIDS group yielded an unexpected finding. These two measures are equivalent to those of the Healthy groups (supplementary analysis Appendix F) and range within average limits. This may explain the loss of power in the comparison between Healthy and Nonhealthy groups.

It was assumed a priori that AIDS patients would not be as anxious as the ARC patients because of having received a diagnosis. ARC constitutes a clinical presentation along the continuum of HIV infection which is situated between asymptomatic and diagnosed AIDS. Since the incubation period of HIV is so lengthy and variable from one individual to another, ARC individuals are faced with an undetermined period of uncertainty regarding their health, and consequently their future. Despite the poor prognosis associated with diagnosis of AIDS, it was felt that the uncertainty, the feeling of being in limbo which accompanies ARC, would prove to be a greater source of tension than being faced with the reality of a terminal illness. The

results obtained on the STAI with this study sample corroborate this impression.

The absence of high anxiety scores (State T-score = 49, Trait T-Score = 53) in the AIDS group can, at first glance, be interpreted as being discrepant with the elevation noted on the Psychasthenia scale of the MMPI (T-score = 63). However, the items of the latter are much more diverse than those of the STAI which specifically refer to anxiety. The items constituting the Psychasthenia scale cover a broader spectrum of symptoms and behaviour. Among others, they include characteristics such as unmanageable or obsessive thoughts, sentiments of apprehension, worriment and/or nervousness, lack of confidence in one's capability, indecisiveness, reports of sadness, physical complaints, and impaired concentration (Graham, 1977). Many of these characteristics may apply to AIDS patients without necessarily arousing feelings of anxiety.

It appears that issues of a psychosocial nature and of psychological adjustment become significant as the individual is no longer experiencing health. In this study sample, asymptomatic seropositive individuals share a profile not unlike that of individuals who have not been infected by HIV. In light of this, the data suggest that HIV sero-positivity per se is not a determining factor in mental/psychological health within this sample of homosexual men, at least at the time of this investigation. Rather,

the psychological and psychosocial implications appear to arise when HIV is no longer latent and compromises the immune system, yielding a wide array of constitutional symptoms, opportunistic infections and/or oncologic manifestations.

Nonetheless, the psychological profile of healthy seropositive individuals may be quite different over time. Levels of anxiety and distress may culminate as the results of positive sero-conversion are given (Leiberich et al., 1989), or when a significant person becomes ill or succumbs to life threatening infections. More studies investigating the coping strategies and the level of adjustment over time are warranted to document the natural course of adjustment. All but one individual constituting the HIV+ group in this study sample were at least one year post seropositive diagnosis at the time of their enrollment and appear to have overcome the initial impact of coping with HIV seropositive testing.

In summary, the magnitude of the psychological turmoil and mood disturbance suffered by the Nonhealthy groups contrasts highly with the level of their neurocognitive faculties. In the latter, although a gradual decline is seen over the continuum of HIV infected groups, the scores nevertheless all remain within normal limits. On the former, only the Healthy groups attained psychological profiles free of pathology and distress.

Relationship between data sets

It appears that both batteries of tests (psychological and neuropsychological) contribute to explain the range of scores achieved to a moderate degree (38% of the variance). However, the predictability of one battery for the results on the other was not considered as being very meaningful with respect to the current results (from 6.3% to 9.6% of predictable variance). One may thus entertain the hypothesis that, not only are neurocognitive signs part of the CNS HIV-related symptom complex, but that personality and affective alterations including apathy and dysphoric mood may be an integral part of the syndrome. Recent observations in human and animal studies have reported associations between specific functions and subcortical structures. For example, mood and motivation are affected by lesions to pathways leading to, or structures such as the striatum and the thalamus (Cummings & Benson, 1989). Thus, the emotional concomitant observed with HIV infection may represent one of the early signs of a chronic subclinical neurological involvement rather than a reaction to neurocognitive disturbance.

Becker, Schaerf, Kingsley, et al. (1989) noted that the presence of physical symptoms rather than affective symptoms was associated with the occurence of cognitive dysfunction. Similarly, Syndulko et al. (1989) reported that the

neuropsychological changes appear to arise in parallel with the emergence of clinically defined immunosuppressed symptoms. Self-reported memory complaints were compared to actual performance on formal assessment. The results indicated that there was only a mild relationship between complaints of decreased memory and definite decrements in scores (Dorfman et al., 1989). However, the frequency of reported lapses correlated significantly with the intensity of mood and/or psychiatric disturbances.

Although Temoshok and her collaborators (Temoshok, Canick, & Sweet, 1989a) interpreted their findings as indicating positive correlations between distress/coping styles and level of impairment of neuropsychological measures, these relationships were only modest. They ranged from r=.19 to r=.31, thus accounting for only 3.6% to 9.6% of the variance. Based on these figures, they concluded that a) cognitive impairment may be exacerbated by distress and certain coping styles, and/or b) that patients react to the awareness of cognitive deficits. However, on two subsequent follow-up assessments approximately 6 and 12 months later, the correlations between neuropsychological and psychological tests were even more negligeable (Temoshok, Drexler, Canick, et al., 1989).

Dysphoric mood or symptoms do not appear to account for impaired neuropsychologic test performance whether sophisticated or simple statistical approaches are applied.

For instance, no significant correlations were uncovered between an expanded Halstead-Reitan Battery and four severity indices of depressed mood (Beck Depression Inventory, Hamilton Rating Scale of Depression, Profile of Mood State, and Symptoms Checklist-90R) (Heaton, Atkinson, Grant, et al., 1989). Advanced statistical approaches were also employed to clarify the relationship between cognitive functions and mood disorder in HIV spectrum disorder. Grant and his co-workers (Grant, Olshen, Atkinson, et al., 1989) employed a recursive partitioning technique according to a decision tree approach. They discovered that self-report measures of depression (POMS) and neuropsychological inefficiency (PASAT) each provided **unique** contributions in the classification of HIV- and HIV+ individuals. In light of these findings, they proposed that dysphoric mood did not account for most of the neurocognitive deficits observed.

Again, in an attempt to dissociate the emergence of neuropsychological dysfunction from mood state, Martin and his colleagues (Martin, Salazar, Kampen, et al., 1989) contrasted the performance of HIV+ patients (asymptomatic and symptomatic) to that of seronegative individuals who presented with adjustment disorders. A wide range of standard and experimental tasks yielded 51 measures. Forty-eight percent of HIV+ individuals were impaired on more than 10 scores and 24% on more than 20; in comparison, only 7%

and 0% of adjustment disorder patients displayed such level of difficulties, respectively.

Should psychological distress be a significant factor in the performance level of neuropsychological tests, intuitively, one would expect that the ARC group would achieve lower scores than the AIDS group as they display greater degrees of turmoil overall. From all of the measures available for both test batteries, the ARC group obtained poorer performance scores than the AIDS group on 57% of the psychological measures and only 13% of the neuropsychological ones.

Thus, it would appear that both psychiatric manifestations and neurocognitive decline become more prominent with the emergence of physical symptoms. However, the psychiatric overlay does not appear to be sufficient to account for the presence of neuropsychological dysfunction. The course of the former appears to be one of a step-wise progression while the latter features a much more gradual and insiduous pattern.

CHAPTER EIGHT

DIRECTIONS FOR FUTURE RESEARCH

Value of screening measures

A review of the literature indicates that there is a wide range of test batteries administered to the patient population under investigation for HIV-related brain disease. Generally centers have employed a comprehensive neuropsychological evaluation, at times including both standard and computerised measures (e.g. Grant et al., 1987, 1988; van Dis, van Beuzekom, de Wolf, & Coutinho, 1989; van Gorp et al., 1989a, 1989b). At the other end of the spectrum, different research groups have attempted to verify the usefulness of brief mental status examination measures in diagnosing and portraying the ADC deficits. For instance, Van Gorp et al. (1989a) found the Mini-Mental Status Exam to have little discriminatitve value in assessing neurological dysfunction in view of the ceiling scores obtained even by the AIDS patients. Another cursory screening measure of mental status, the Neurobehavioral Cognitive Status Examination (NBCSE), was systematically compared to a more comprehensive assessment in AIDS patients and normal controls (Kobayashi et al., 1989). Results indicated a lack of sensitivity in evaluating impairment across multiple functional areas. While it could identify memory deficits in a small proportion of patients (7 of 31),

other cognitive deficits were detected in more than half of the patients (17 of 31) when a more extensive but limited battery of tests was administered.

Finally, other investigators have opted for an intermediary approach and conducted screening evaluations with a subset of tests which were deemed proficient at illustrating the presumed clinical profile of the ADC (Connolly, Tovey & Gazzard, 1989; Fernadez et al., 1989; Morriss, Schaerf, Brandt, et al., 1989). In such cases, test protocols typically comprised measures of motor functions (e.g. Purdue Pegboard, Finger Tapping, Timed Gait) and psychomotor speed (e.g. Trail Making, Digit Symbol, Symbol Digit Modalities). In some instance, these selective measure were subsequently complemented by a supplementary series of tests evaluating various aspects of memory (e.g. Sidtis et al., 1989). Based on a wider test protocol, Boccellari, Davis, and Dilley (1989) identified a specific subset of neuropsychological tests to detect neurocognitive deficits in AIDS patients. They found that an overall neuropsychological impairment index could be predicted by three measures with 87% of the variance accounted for. These consisted of Trail Making B, Finger Tapping Test, and Visual Reproductions (from the Wechsler Memory Scale).

In a setting where clinical demands are elevated, the first appoach mentioned above is certainly overly time-consuming and may not be the most appropriate and cost

effective. Futhermore, from a reseach point of view, the more test scores there are, the larger the samples under investigation should be in order to have acceptable subject-to-variable ratio in multivariate data analyses. In contrast, the use of only brief screening measures is likely to produce a fair proportion of false negative scores (i.e. no evidence of deficits when they are present) which may lead to improper management from a clinical perspective, and inconsequential findings at the research end. Intuitively, the latter approach appears to be the most appropriate for both clinical and research dimensions. Expediency and proper clinical examination are thus amalgamated to allow for meaningful evaluations of ADC, its presenting symptomatology, and empirical investigations towards a better understanding of the syndrome. Research groups should aim to adopt common test protocols in order to facilitate comparisons between studies, and avert discordant results.

Choice of deficit cut-off scores

One of the reasons why discrepant findings are reported in the literature stems from the fact that different deficit cut-off scores are used by the various investigative groups. These have extended from 1 standard deviation (SD) below normative and/or sample means (Grant et al., 1987 & 1988; Tomoshok et al., 1989) to 1.5 SD (Selnes et al., 1989), and

2 SD (Miller et al., 1989). Here again, it would be advisable to determine and employ one specific value systematically across all studies, otherwise, comparisons between different research teams are difficult to integrate.

From a clinical point of view, limiting normal skill ratings within a standard deviation from the mean may be too stringent a criterion and allows for little interindividual variability in performance. Scores falling between 1 and 2 SD from the norm reflect low average to borderline levels of achievement which may be difficult to account for and have various sources of etiologies. Thus, it would appear more rigorous and parsimonious to use 2 SD from the mean as a deficit cut-off score. In keeping with this, Belsky-Barr et al. (1989) provided a breakdown of the distribution of individuals whose scores exceeded from 1 to 5 SD below the sample means. They found that the proportion of HIV+ and HIV- individuals which obtained scores greater than 1 SD were equivalent (i.e. 18 of 32 and 15 of 18, respectively). In contrast, 14 HIV+ and only 3 HIV- had measures surpassing 2 SD.

From a research perspective, it becomes abstruse when mean group scores falling within normal limits are statistically distinct from each other, and cannot be attributed to differences in demographic, epidemiologic, and attribute variables. Thus, although a significant impairment cannot be diagnosed from a clinical point of

view, this statistical neurocognitive difference between otherwise comparable groups would suggest that a mild decline in neurocognitive functions is being experienced, and must be investigated over time to determine any alteration in performance level.

Longitudinal studies

Based on the observation that there are no more outliers on neuropsychological tests when age, education, and mood are used as covariates, Satz (1989) suggested that early reports may have been too hasty in ascribing neuropsychological abnormalities to HIV infection. Thus, he proffered that HIV may be neurotropic but not necessarily neuropathogenic in nature. Longitudinal studies will serve to elucidate this issue. At the moment, only a few preliminary investigations have presented their findings on short follow-up intervals.

For example, over a nine month period, deteriorations in neurocognitive measures were observed in 15 of 66 HIV symptomatic individuals, while 25 of 66 revealed marked improvement and 26 of 66 showed a mixture of mild changes in both direction (Temoshok et al, 1989b). although AZT treatment may provide a plausible explanation for improvement in functioning, those patients who exhibited declines also used AZT. Practice effects and changes in psychosocial distress measures were also considered to be

contributory factors in the decay of performance. Similarly, Katlama, Duneton, Chieze, et al. (1989) reported variable findings over a six months follow-up in a very small sample: while 6 of 10 displayed stable performance, 3 improved and 1 deteriorated.

Generally, seronegative controls, asymptomatic HIV+, and seroconverters (i.e. those changing from HIV- to HIV+ during the inter-test interval) displayed no evidence of altered abilites over 6 to 12 months time (Grant, Heaton, Jernigan, et al, 1989; Miller, Selnes, Visscher, et al; 1989; Visscher, Miller, Satz, et al., 1989). Moreover, no significant decline was seen in a subset of asymptomatic HIV+ who all displayed AIDS defining symptoms by the time of their reassessment (Selnes, et al., 1989c). In this particular sample (MACS), there had been no difference between seronegative and AIDS patient groups on both testing. In contrast, a significant proportion of AIDS patients experienced failures on neuropsychological screening tests, and complained of more neurological symptoms at each follow-up assessments (Grant et al.,1989; Visscher et al., 1989). In one reseach group in particular, the Trail Making test has been considered to be a sensitive longitudinal measure of neurocognitive decline associated with HIV infection (Miller et al., 1989c). Their examination of repeated performance scores extending to 6 semi-annual assessment intervals indicated that deficits on

this test become apparent only after the initial AIDS diagnosis (Miller et al., 1989c).

The findings described above are still premature and inconclusive. Replications of results, longer re-evaluation periods and larger sample sizes are thus warranted in order to shed light on the long-term pathogenesis of potential HIV encephalopathy.

Multidisciplinary correlative studies

A new direction for correlative studies is evolving with investigations examining the relationship between immunological or CSF parameters and neuropsychological observations. One area of pursuit in longitudinal studies has been to determine whether any CSF alterations can predict overt neurobehavioural and/or neurocognitive symptoms. It was observed that, in comparison to symptomatic HIV+ individuals without neurological features, the ones who do present with neurological signs show a) greater elevations in immunoglobulin-G (IgG), Beta-2 microglubulins and percentage of HIV isolation, b) reduced albumin, and c) evidence of intratechal synthesis of IgG (Zeriav, Jevtovic, Brmbolic, et al., 1989). These changes in CSF markers may reflect greater HIV activation within the CNS (Singer, Syndulko, Ruane, et al., 1989). In particular, Signer and his collaborators found greater p24 concentration, higher pleocytosis, and more intra-blood

brain barrier IgG synthesis rate in HIV+ individuals with neurologic manifestations such as CNS motor signs and/or moderate to severe dementia.

Another avenue of investigation is the quantification of immunoglobulins G, A, and M in order to discriminate HIV encephalitis from opportunistic brain infection in AIDS patients presenting with neurological syndromes (Luer, Poser, Rogler, et al., 1989). The production of local IgA (42%), and IgM (48%) was associated with opportunistic infections and not observed in HIV encephalitis. In contrast, IgG production was seen in both HIV infection (28%) and opportunistic infections (36%).

Similarly, elevations in CSF neopterin and B2-microglobulin are frequently observed in HIV infected individuals and are considered a non-specific finding as they are reported with opportunistic infection, neoplasms, and encephalopathy (Brew, Bhalla, Paul, et al., 1989a, 1989b; Goebel, Bogner, Junge-Hulsing, et al., 1989). Nevertheless, a significant correlation was noted between levels of CSF neopterin or B2-microglobulin and the severity of ADC in patierts free of other confounding independent neurological involvement (Brew et al., 1989a; Brew, Bhalla, Schwartz & Price, 1989b). In addition, B2-microglobulin markers appear to serve as a useful monitor of AZT therapeutic responses (Brew et al., 1989a).

At the present, no clear association has been detected between cognitive dysfunction and immunological status markers such as white blood cells, total T lymphocytes, T4, and T4:T8 ratio despite advanced HIV infection (ARC and AIDS). Fernandez and colleagues (1989) reported that AIDS and ARC patients achieved comparable neurocognitive performance scores but revealed immunological variables which differed markedly. In contrast, Dilley et al. (1989) found low but significant correlations between speed of information processing, higher abstract reasoning, fine motor speed and T8 cells. They also reported an association between measures of verbal ability and T4 cells.

More and more, research is combining the biomedical and brain-behaviour dimensions of AIDS in an attempt to identify the association between HIV-CNS manifestation and indices generally reflective of HIV systemic progression. The goal is to achieve a better understanding of the deadly disease and discover the ultimate solution for its cure or its proper management. "*ADC has emerged as a major clinical problem and HIV brain infection as a central biological aspect of the AIDS retrovirus*" (Price et al., 1988).

CHAPTER NINE

CONCLUSIONS

Despite a plethora or research studies, we have only achieved a glimpse of the phenomena associated with HIV infection. Many issues still need to be resolved more comprehensively. From a neurological/neuropsychological perspective, they include the role of the brain in HIV disease, the CNS-related sequelae of the virus, and the impact of these sequealae in further development and therapeutic management of the illness. The time course at which the virus infiltrates the brain during the infection remains unclear. Improvements in assessment techniques and close monitoring of the neuropsychological manifestations may contribute to a better understanding of the mechanisms by which CNS functions are compromised and to what extent these may have repercussions on the progression of the disease. Should the CNS effects be independent of the immune system, it may still be possible to detect the presence of the disease before the appearance of immune-related symptomatology. For example, if alterations in emotionality are associated with evolution of the disease, it would be possible to identify passage of one disease stage to another. It has been recognized that certain immune system transmitters can activate certain neuropeptides, and certain neurotransmitters can in turn

regulate the progression of an immune response through a direct or indirect mechanism (Hall, McGillis, Spangelo & Goldstein, 1985). Furthermore, a subset of these neurotransmitters and peptides are known to predispose personality states and traits associated with behaviour. Thus, should AIDS result in distinct brain aberrations and pattern(s) of neuropsychological deficits be linked to behavioural correlates, observations of neurobehavioural changes may reflect the CNS deficits.

The current study has attempted to shed some light and contribute to a better understanding of the ADC, a most portentous aspect of HIV infection. This neurological complication is known to arise at any time during the course of the disease. On the one hand, it may appear as the presenting symptom and prevail during the course of the illness. On the other, it may accompany and exacerbate constitutional ailments. As it progresses, it ultimately affects work, life activities, and self-care, thus having a large impact on the individual and on society. Gradually, the individual becomes increasingly disabled, ceases to be a productive member, and requires expensive long-term assistance and/or institutional care.

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Appendix A-1

Statement of Intent

The goal of this research is to arrive at a better understanding of AIDS and the effect of the AIDS virus on the cognitive and mental abilities of those affected by the disease. Your participation will provide important information toward this end.

You will be administered a series of tests assessing various functions such as memory, language, attention, concentration, verbal and nonverbal reasoning, motor and sensory functions. You will also be given questionnaires which will provide information regarding your mood, health, and general personality characteristics. The whole procedure should take about a day (6 to 6.5 hours). There will be a one hour lunch break, and short rest periods (15 minutes) during the morning and afternoon sessions. The assessment may be broken into 2 or 3 sessions over consecutive days. I will attempt to the best of my ability to answer all questions you may have, either as they arise, or at the end of the testing session.

Your identity will be known only to the investigator and your anonymity will be protected by matching your test file and results with an identification number. Only the investigator will have access to the list that matches your name to the identification number. Once the results have been analyzed and the study finished, the key list will be destroyed.

You have the right to stop at any time during the testing session and withdraw your participation.

Do you understand?

Do you have any questions?

Appendix B-1

Consent Form

I _____, having freely volunteered my time and participation in this study, do hereby agree to its conditions. I have been told that the confidentiality of the test results will be safeguarded and that my anonymity will be protected by the investigator. I also give my permission to have medical information on myself released to the investigator. I have read the statement of intent and I understand the extent and limits of my participation in this study. I have read and/or listened to the above.

Signature of participant: _____

Signature of investigator: _____

Date: _____

I _____, give my permission to release the results of the neuropsychological assessment performed on myself to _____.

Signature of participant: _____

Signature of investigator: _____

Date: _____

Appendix C-1

Frequency Analysis of Age

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
Age	**Absolute Frequency**	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
< 33	15	48.4	17	60.7
> 33	16	51.6	11	39.3

Appendix C-2

Frequency Analysis of Education

(N = 59)

	Healthy (n = 31)		**Nonhealthy** (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
< Gr. 13	13	41.9	19	67.9
> Gr. 13	18	58.1	9	32.1

Appendix C-3

Frequency Analysis of Occupational Status

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Employed	23	74.2	9	32.1
Unemployed	5	16.1	19	67.9
Student	3	9.7	0	0.0

Appendix C-4

Frequency Analysis of Recreational Drug Use

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Ingestion of Drugs				
Yes	28	90.3	28	100.0
No	3	9.7	0	0.0
Pattern of Intake				
Experim.	9	29.0	4	14.3
Reg/Spor.	22	71.0	24	85.7
Use at Assessment				
Yes	13	41.9	9	32.1
No	18	58.1	19	67.9

Appendix C-5

Frequency Analysis of Recreational Drug Type

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Hallucinogens				
Yes	17	54.8	23	82.1
No	14	45.2	5	17.9
Narcotics				
Yes	2	6.5	6	21.4
No	29	93.5	22	78.6
Stimulants				
Yes	13	41.9	18	64.3
No	18	58.1	10	35.7
Depressants				
Yes	3	9.7	3	10.7
No	28	90.3	25	89.3
Cannabis				
Yes	28	90.3	28	100.0
No	3	9.7	0	0.0
Poppers				
Yes	12	38.7	17	60.7
No	19	61.3	11	39.3

Appendix C-6

Frequency Analysis of Alcohol Intake

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Social Ingestion				
Yes	29	93.5	23	82.1
No	2	6.5	5	17.9
Temporary Abuse				
Yes	8	25.8	7	25.0
No	23	74.2	21	75.0
Use at Assessment				
Yes	29	93.5	17	60.7
No	2	6.5	11	39.3

Appendix C-7

Frequency Analysis of Medical Symptoms

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Non-HIV Symptoms				
Yes	9	29.0	5	17.9
No	22	71.0	23	82.1
CNS-related Symptoms				
Yes	2	6.5	10	35.7
No	29	93.5	18	64.3
Sexually Transmited Diseases				
Yes	10	32.3	16	57.1
No	21	67.7	12	42.9

Appendix C-8

Frequency Analysis of Prescribed Medication

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
CNS				
Yes	10	32.3	16	57.1
No	21	67.7	12	42.9
Autonomic/Cardiovascular				
Yes	7	22.6	4	14.3
No	24	77.4	24	85.7

Appendix C-9

Frequency Analysis of Mental Health Interventions

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
	Absolute Frequency	**Relative Frequency (%)**	**Absolute Frequency**	**Relative Frequency (%)**
Use of services				
Yes	18	58.1	19	67.9
No	13	41.9	9	32.1

Appendix D-1

Frequency Analysis of Age

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Age	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
< 33	8	47.1	7	50.0	11	78.6	6	42.9
> 33	9	52.9	7	50.0	3	21.4	8	57.1

Appendix D-2

Frequency Analysis of Education

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Fre	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
< Gr. 13	8	47.1	5	35.7	10	71.4	9	64.3
> Gr. 13	9	52.9	9	64.3	4	28.6	5	35.7

Appendix D-3

Frequency Analysis of Occupational Status

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
Employed	13	76.5	10	71.4	7	50.0	2	14.3
Unemployed	2	11.8	3	21.4	7	50.0	12	85.7
Student	2	11.8	1	7.1	0	0.0	0	0.0

Appendix D-4

Frequency Analysis of Recreational Drug Use

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
Ingestion of Drugs								
Yes	14	82.4	14	100.0	14	100.0	14	100.0
No	3	17.6	0	0.0	0	0.0	0	0.0
Pattern of Intake								
Exp.	8	47.1	1	7.1	2	14.3	2	14.3
Reg/Spor.	9	52.9	13	92.9	12	85.7	12	85.7
Use at Assessment								
Yes	5	29.4	8	57.1	5	35.7	4	28.6
No	12	70.6	6	42.9	9	64.3	10	71.4

Appendix D-5

Frequency Analysis of Recreational Drug Type

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
Hallucinogens								
Yes	6	35.3	11	78.6	12	85.7	11	78.6
No	11	64.7	3	21.4	2	14.3	3	21.4
Narcotics								
Yes	0	0.0	2	14.3	3	21.4	3	21.4
No	17	100.0	12	85.7	11	78.6	11	78.6
Stimulants								
Yes	5	29.4	8	57.1	11	78.6	7	50.0
No	12	70.6	6	42.9	3	21.4	7	50.0
Depressants								
Yes	0	0.0	3	21.4	1	7.1	2	14.3
No	17	100.0	11	78.6	13	92.9	12	85.7
Cannabis								
Yes	14	82.4	14	100.0	14	100.0	14	100.0
No	3	17.6	0	0.0	0	0.0	0	0.0
Inhalant Nitrates								
Yes	5	29.4	7	50.0	7	50.0	10	71.4
No	12	70.6	7	50.0	7	50.0	4	28.6

Appendix D-6

Frequency Analysis of Alcohol Intake

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
Social Ingestion								
Yes	16	94.1	13	92.9	10	71.4	13	92.9
No	1	5.9	1	7.1	4	28.6	1	7.1
Temporary Abuse								
Yes	5	29.4	3	21.4	6	42.9	1	7.1
No	12	70.6	11	78.6	8	57.1	13	92.9
Use at Assessment								
Yes	17	100.0	12	85.7	9	64.3	8	57.1
No	0	0.0	2	14.3	5	35.7	6	42.9

Appendix D-7

Frequency Analysis of Medical Symptoms

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**	**Abs Freq**	**Rel Freq (%)**
Non-HIV Symptoms								
Yes	3	17.6	6	42.9	5	35.7	0	0.0
No	14	82.4	8	57.1	9	64.3	14	100.0
CNS-related Symptoms								
Yes	1	5.9	1	7.1	6	42.9	4	28.6
No	16	94.1	13	92.9	8	57.1	10	71.4
Sexually Transmited Diseases								
Yes	4	23.5	6	42.9	8	57.1	8	57.1
No	13	76.5	8	57.1	6	42.9	6	42.9

Appendix D-8

Frequency Analysis of Prescribed Medication

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)
CNS								
Yes	4	23.5	6	42.9	9	64.3	7	50.0
No	13	76.5	8	57.1	5	35.7	7	50.0
Autonomic/Cardiovascular								
Yes	4	23.5	3	21.4	4	28.6	0	0.0
No	13	76.5	11	78.6	10	71.4	14	100.0

Appendix D-9

Frequency Analysis of Mental Health Interventions

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)	Abs Freq	Rel Freq (%)
Use of services								
Yes	7	41.2	11	78.6	11	78.6	8	57.1
No	10	58.8	3	21.4	3	21.4	6	42.9

Appendix E.1

WAIS-R Subtest Scores of the Total Sample

(N = 59)

Subtests	Mean	SD	Minimum	Maximum
Information	12.29	2.68	7.00	18.00
Digit Span	9.81	2.81	5.00	18.00
Vocabulary	12.32	2.60	7.00	18.00
Arithmetic	10.83	2.48	7.00	17.00
Comprehension	13.25	2.46	8.00	19.00
Similarity	11.97	2.33	6.00	16.00
Picture Completion	10.88	1.80	6.00	14.00
Picture Arrangement	11.69	2.88	7.00	17.00
Block Design	11.17	2.49	5.00	17.00
Object Assembly	10.36	2.50	4.00	15.00
Digit Symbol	9.49	2.47	5.00	16.00

Appendix E.2

WAIS-R Subtest Scores of Groups by Health Status

(N = 59)

	Healthy (n = 31)		Nonhealthy (n = 28)	
Subtests	**Mean**	**SD**	**Mean**	**SD**
Information	12.97	2.60	11.54	2.60
Digit Span	10.16	2.78	9.43	2.83
Vocabulary	13.29	2.51	11.25	2.30
Arithmetic	11.06	2.14	10.57	2.83
Comprehension	13.77	2.62	12.68	2.18
Similarity	12.35	2.35	11.54	2.28
Picture Completion	10.93	1.82	10.82	1.81
Picture Arrangement	11.77	3.02	11.61	2.78
Block Design	11.58	2.70	10.71	2.19
Object Assembly	10.39	2.60	10.32	2.42
Digit Symbol	10.13	2.40	8.79	2.39

Appendix E.3

WAIS-R Subtest Scores of Groups by Medical Diagnosis

(N = 59)

	HIV- (n = 17)		HIV+ (n = 14)		ARC (n = 14)		AIDS (n = 14)	
Subtests	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Information	13.23	2.44	12.64	2.84	11.86	2.14	11.21	3.04
Digit Span	10.76	2.68	9.43	2.85	9.57	3.23	9.29	2.49
Vocabulary	13.71	2.54	12.79	2.45	11.57	2.38	10.93	2.27
Arithmetic	11.41	2.09	10.64	2.20	10.93	2.79	10.21	2.94
Comprehension	14.12	2.52	13.36	2.76	12.71	1.86	12.64	2.53
Similarity	12.18	2.63	12.57	2.03	11.71	2.55	11.36	2.06
Picture Comp.	10.94	1.56	10.93	2.16	11.36	1.51	10.29	2.20
Picture Arr.	13.06	2.95	10.21	2.36	12.21	3.04	11.00	2.45
Block Design	11.88	2.47	11.21	3.02	11.36	2.31	10.07	1.94
Object Assem.	10.12	2.34	10.71	2.95	11.50	1.70	9.14	2.51
Digit Symbol	9.94	2.56	10.36	2.27	8.86	2.07	8.71	2.76

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            This files contains the commands which describe
            FFAS's PH.D. dissertation data.
            The file includes:
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                .VARIABLE NAMES
                .VARIABLE LABELS
            Each case in the data file consists of
            5 records....
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                2nd Rey-Osterrieth, RNVLT, PASAT, CCC
                    Trails, Visual Search, & HVOT
                3rd Facial Recognition, Verbal Fluency
                    Boston Naming, Tokens, 2D-Stereognosis
                    R-L Orientation, Lateral Dominance,
                    Finger Localisation, Dynamometer,
                    Finger Tapping, & STAI
                4th SIP & MMPI
                5th Interview data
             The results of this descriptive run are saved
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          VOCAB 29-30   ARITH 31-32   COMP 33-34
          SIMIL 35-36   PCOMPL 37-38   PICARR 39-40
          BDESIGN 41-42   OBJASS 43-44   DSYMBOL 45-46
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          RAVLTA3 65-66   RAVLTA4 67-68   RAVLTA5 69-70
          RAVLTB1 71-72   RAVLTA6 73-74   RAVLTRGN 75-76
          RAVLTRCL 77-78

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           RLREVERS 35-36   RLATDOM 38-39   LLATDOM 40-41
           BLATDOM 42   PRFLOC 44-45   NPRFLOC 46-47
           PRDYNAM 49-52(2)   NPRDYNAM 53-56(2)
           PRFTAP 58-60(1)   NPRFTAP 61-63(1)
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           STAIT100 72-74

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           PSYINT 15   AUTOCARD 17   ENDOCR 18   CNSDRUGS 19
           HIVDRUGS 20   STD 22   NONHIV 23   HIVSYMPY 24
           CNSSYMPT 25   WORK 27

FORMAT EDUCAT WMSA1 WMSB1 WMSA2 WMSB2 REYCOPY REYRECAL HVOT
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       SIPA SIPAB SIPC SIPW SIPRP SIPE (F3.1)
       PASATT24 PASATT20 PASATT16 PASATT12 (F2.1)
       PRDYNAM NPRDYNAM (F4.2)

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COMPUTE STEREOG=(PR2DTIME+NPR2DTME)
COMPUTE FINGLOC=(PRFLOC+NPRFLOC)
COMPUTE WMS1=(WMSA1+WMSB1)/2
COMPUTE WMS2=(WMSA2+WMSB2)/2
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COMPUTE VSAVE=VSTOT/4
COMPUTE WFTOT=FLUENCYF+FLUENCYA+FLUENCYS+FLUENCYC
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COMPUTE SIPSDII=((SIPEB+SIPSI+SIPAB+SIPC)/365.7)*100
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COMPUTE SIPTOTB=SIPA+SIPAB+SIPC+SIPW+SIPRP+SIPE
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COMPUTE MMPISUM1=MMPIHS+MMPID+MMPIHY
COMPUTE MMPISUM2=MMPIPD+MMPIMA
COMPUTE MMPISUM3=MMPIPT+MMPISC

VARIABLE LABELS
   GROUP       "PATIENT GROUP CLASSIFICATION"
   SSNUMBER    "SUBJECT IDENTIFICATION NUMBER"
   STATUS      "HEALTHY VS NONHEALTHY"
   AGE         "AGE IN YEARS"
   EDUCAT      "EDUCATION IN YEARS"
   DIAGTIME    "TIME SINCE DIAGNOSIS IN MONTHS"
   FSIQ        "FULL SCALE IQ"
   VIQ         "VERBAL IQ"
   PIQ         "PERFORMANCE IQ"
   INFO        "INFORMATION"
   DSPAN       "DIGIT SPAN"
   VOCAB       "VOCABULARY"
   ARITH       "ARITHMETIC"
   COMP        "COMPREHENSION"
   SIMIL       "SIMILARITY"
   PCOMPL      "PICTURE COMPLETION"
   PICARR      "PICTURE ARRANGEMENT"
   BDESIGN     "BLOCK DESIGN"
   OBJASS      "OBJECT ASSEMBLY"
   DSYMBOL     "DIGIT SYMBOL"
   WMSA1       "WMS STORY A - IMMEDIATE RECALL"
   WMSB1       "WMS STORY B - IMMEDIATE RECALL"
   WMSA2       "WMS STORY A - DELAYED RECALL"
   WMSB2       "WMS STORY B - DELAYED RECALL"
   RAVLTA1     "REY AUDITORY VERBAL LEARNING - TRIAL 1"
   RAVLTA2     "REY AUDITORY VERBAL LEARNING - TRIAL 2"
   RAVLTA3     "REY AUDITORY VERBAL LEARNING - TRIAL 3"
   RAVLTA4     "REY AUDITORY VERBAL LEARNING - TRIAL 4"
   RAVLTA5     "REY AUDITORY VERBAL LEARNING - TRIAL 5"
   RAVLTB1     "REY AUDITORY VERBAL LEARNING - LIST B"
   RAVLTRGN    "REY AUDITORY VERBAL LEARNING - RECOGNITION"
   RAVLTA6     "REY AUDITORY VERBAL LEARNING - TRIAL 6"
   RAVLTRCL    "REY AUDITORY VERBAL LEARNING - DELAYED RECALL"
   REYCOPY     "REY OSTERRIETH FIGURE - COPY"
   REYRECAL    "REY OSTERRIETH FIGURE - RECALL"
   RNVLT1      "REY NONVERBAL LEARNING - TRIAL 1"
   RNVLT2      "REY NONVERBAL LEARNING - TRIAL 2"
   RNVLT3      "REY NONVERBAL LEARNING - TRIAL 3"
   RNVLT4      "REY NONVERBAL LEARNING - TRIAL 4"
   RNVLT5      "REY NONVERBAL LEARNING - TRIAL 5"
   RNVLTRGN    "REY NONVERBAL LEARNING - RECOGNITION"
   RNVLTRCL    "REY NONVERBAL LEARNING - DELAYED RECALL"
   PASATS24    "PASAT SCORE AT SPEED 2.4"
   PASATS20    "PASAT SCORE AT SPEED 2.0"
   PASATS16    "PASAT SCORE AT SPEED 1.6"
   PASATS12    "PASAT SCORE AT SPEED 1.2"
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PASATT24	"PASAT TIME AT SPEED 2.4"
PASATT20	"PASAT TIME AT SPEED 2.0"
PASATT16	"PASAT TIME AT SPEED 1.6"
PASATT12	"PASAT TIME AT SPEED 1.2"
CCCTRI0	"CONSONANT TRIGRAMS AT 0"
CCCTRI3	"CONSONANT TRIGRAMS AT 3"
CCCTRI9	"CONSONANT TRIGRAMS AT 9"
CCCTRI18	"CONSONANT TRIGRAMS AT 18"
TRAILAT	"TRAIL MAKING A - TIME"
TRAILAC	"TRAIL MAKING A - CREDITS"
TRAILBT	"TRAIL MAKING B - TIME"
TRAILBC	"TRAIL MAKING B - CREDITS"
TRAILBE	"TRAIL MAKING B - ERRORS"
VSEARCHA	"VISUAL SEARCH - BLOC A"
VSEARCHB	"VISUAL SEARCH - BLOC B"
VSEARCHC	"VISUAL SEARCH - BLOC C"
VSEARCHD	"VISUAL SEARCH - BLOC D"
HVOT	"HOOPER VISUAL ORGANIZATION TEST"
FACRECOG	"BENTON'S TEST OF FACIAL RECOGNITION"
FLUENCYF	"WORD FLUENCY - F"
FLUENCYA	"WORD FLUENCY - A"
FLUENCYS	"WORD FLUENCY - S"
FLUENCYC	"WORD FLUENCY - CORRECTION"
NAMING	"BOSTON NAMING TEST"
TOKENS	"TOKEN TEST"
PR2DFIG	"STEREOGNOSIS - PREFERED HAND SCORE"
PR2DTIME	"STEREOGNOSIS - PREFERED HAND TIME"
NPR2DFIG	"STEREOGNOSIS - NONPREFERED HAND SCORE"
NPR2DTME	"STEREOGNOSIS - NONPREFERED HAND TIME"
RLORIENT	"RIGHT-LEFT ORIENTATION"
RLREVERS	"RIGHT-LEFT REVERSAL SCORE"
RLATDOM	"LATERAL DOMINANCE - RIGHT"
LLATDOM	"LATERAL DOMINANCE - LEFT"
BLATDOM	"LATERAL DOMINANCE - BOTH"
PRFLOC	"FINGER LOCALIZATION - PREFERED"
NPRFLOC	"FINGER LOCALIZATION - NONPREFERED"
PRDYNAM	"DYNAMOMETER - PREFERED"
NPRDYNAM	"DYNAMOMETER - NONPREFERED"
PRFTAP	"FINGER TAPPING - PREFERED"
NPRFTAP	"FINGER TAPPING - NONPREFERED"
STAIST	"STATE-TRAIT ANXIETY INVENTORY - STATE T SCORE"
STAIS100	"STATE-TRAIT ANXIETY INVENTORY - STATE PERCENTILE"
STAITT	"STATE-TRAIT ANXIETY INVENTORY - TRAIT T SCORE"
STAIT100	"STATE-TRAIT ANXIETY INVENTORY - TRAIT PERCENTILE"
SIPSR	"SIP - SLEEP & REST"
SIPEB	"SIP - EMOTIONAL BEHAVIOR"
SIPBCM	"SIP - BODY CARE MOVEMENT"
SIPHM	"SIP - HOME MANAGEMENT"
SIPM	"SIP - MOBILITY"
SIPSI	"SIP - SOCIAL INTERACTION"
SIPA	"SIP - AMBULATION"
SIPAB	"SIP - ALERT BEHAVIOR"

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    SIPC        "SIP - COMMUNICATION"
    SIPW        "SIP - WORK"
    SIPRP       "SIP - RECREATION & PASSTIME"
    SIPE        "SIP - EATING"
    MMPIL       "MMPI - LIE VALIDITY SCALE"
    MMPIF       "MMPI - F VALIDITY SCALE"
    MMPIK       "MMPI - K VALIDITY SCALE"
    MMPIHS      "MMPI - HYCHODRIASIS"
    MMPID       "MMPI - DEPRESSION"
    MMPIHY      "MMPI - HYSTERIA"
    MMPIPD      "MMPI - PSYCHOPATHIC DEVIATION"
    MMPIMF      "MMPI - MALE/FEMALE"
    MMPIPA      "MMPI - PARANOIA"
    MMPIPT      "MMPI - PSYCHASTENIA"
    MMPISC      "MMPI - SCHIZOPHRENIA"
    MMPIMA      "MMPI - HYPOMANIA"
    MMPISI      "MMPI - SOCIAL ISOLATION"
    TRAILS      "TRAIL A + TRAIL B (TOTAL TIME)"
    STEREOG     "STEREOGNOSIS - PREFERED + NONPREFERED HANDS (TIME)"
    FINGLOC     "FINGER LOCALIZATION - PREFERED + NONPREFERED HANDS"
    WMS1        "WMS STORIES - IMMEDIATE RECALL"
    WMS2        "WMS STORIES - DELAYED RECALL"
    RAVLTTOT    "RAVLT TOTAL TRIALS OF LIST A"
    RNVLTTOT    "RNVLT TOTAL OF FIVE IMMEDIATE RECALL TRIALS"
    PASATSTO    "PASAT - TOTAL CORRECT SCORE"
    PASATTOT    "PASAT - TOTAL TIME SCORE"
    PASATAVE    "PASAT - MEAN TIME SCORE (4 TRIALS)"
    CCCTOT      "CONSONANT TRIGRAMS TOTAL SCORE"
    VSTOT       "VISUAL SEARCH - TOTAL OF 4 BLOCS"
    VSAVE       "VISUAL SEARCH - AVERAGE OF 4 BLOCS"
    WFTOT       "WORD FLUENCY SCORE"
    SIPSDI      "SIP - PHYSICAL SCORE"
    SIPSDII     "SIP - PSYCHOSOCIAL SCORE"
    SIPTOT      "SIP - TOTAL SCORE"
    LATDOM      "LATERAL DOMINANCE SCORE"
    MMPISUM1    "MMPI - SUM OF HY D & HY"
    MMPISUM2    "MMPI - SUM OF PD & MA"
    MMPISUM3    "MMPI - SUM OF PT & SC"

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