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Psychoneuroimmunology and Healing Touch in HIV Disease

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ABSTRACT

PSYCHONEUROIMMUNOLOGY AND HEALING TOUCH IN HIV DISEASE

By Jo Lynne Wheeler Robins, Ph.D., RN

The purpose of this study was to ascertain the effects of Healing Touch (HT) on well-being and neuroendocrine function in individuals living with HIV disease. A total of 27 males completed the 4-week HT intervention. Each weekly HT session lasted 30 minutes and consisted of only the chakra connection. Because of the small sample size and the impact of gender on neuroendocrine and immune function, women were not included in this study. Dependent variables included well-being as measured by three well-being and two psychological distress instruments, serum serotonin, salivary DHEA and cortisol, and a variety of enumerative and functional measures of immune function. A pretest-posttest design experimental design including a wait-list control group was used. Multivariate analysis of covariance was used to test the research hypotheses followed by univariate analysis of variance to detect the contribution of individual variables to the overall multivariate models. It was hypothesized that HT would increase participant well-being, serum serotonin and salivary DHEA; decrease salivary cortisol; and improve immune function in individuals living with HIV disease. All of the research hypotheses were rejected. Discussion of the results as well as directions for future research are presented.

Chapter 1

Introduction

Psychoneuroimmunology (PNI) is the study of the complex relationships among behavior and the neuroendocrine and immune systems. Bi-directional communication pathways exist between the neuroendocrine and immune systems. In humans, it is thought that certain behaviors affect these interactions and ultimately health outcomes (Ader, 1992; Ader, Cohen, & Felton, 1995; Black, 1995). PNI is an outgrowth of research done over 40 years ago exploring the effects of stress on the immune system. In the late 1970's the discovery of endorphins and their role in endogenous pain control was pivotal in the emergence of psychoneuroimmunology as a significant field of study (Poole, 1993). Evidence suggests that endorphins as well as other chemicals produced by the neuroendocrine and immune systems are part of an intricate mind-body network operating to preserve health and mediate disease processes (Black, 1994; Dossey, Keegan, Guzzetta, & Kolkmeier, 1995).

Peptides in the form of neurotransmitters, for example, mediate intercellular communication throughout the brain and body. These peptides and their receptors are the "biochemical correlates of emotions" (Pert, 1993, p. 178). According to Pert, the discovery of mood-altering chemicals that interact with the immune system implies that it should be possible for individuals to achieve a mental state that positively affects the immune system.

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A variety of therapies, including energy therapies, such as healing touch, may have the potential to induce a mental state conducive to enhanced immune function. For thousands of years, in eastern as well as western thought, the human body has been conceptualized as an energy field. It is conceived as a manifestation of universal energy, the basic constituent and source of all life. The human energy field (HEF) is a "luminous body that surrounds and interpenetrates the physical body, emits its own characteristic radiation and is usually called the aura" (Brennan, 1987, p.41). The HEF or aura is comprised of seven layers, with each layer having its own particular appearance and function. Each layer contains chakras, which are essentially energy vortexes that connect the HEF to the environmental and universal energy fields. Each chakra is thought to correspond to a specific endocrine gland and particular area of the body. One of the primary functions of the chakras is to vitalize and energize the HEF and physical body. Energy-based therapies have been developed that allow assessment and manipulation of the HEF to enhance health and well-being. Healing touch (HT) is an energy-based therapeutic technique theorized to influence the chakras and human energy field ultimately to impact physical, psychological, and spiritual health and well-being (Dossey et al., 1995).

HT is theorized to elicit effects through an energy exchange between practitioner and recipient. However, direct measurement of this energy exchange is not currently possible. Research to date on energy therapies has focused on various indirect measures of psychological and physiological effects thought to be involved in mind-body interactions. Psychoneuroimmunology provides a well-studied framework for investigating and understanding the intricacies and significance of the relationship between the mind and the body. In this research, the PNI conceptual framework was used as the foundation for a

clinical trial examining the effects of HT on the psychological parameter of well-being; the neuroendocrine parameters of bioavailable serum serotonin, salivary dehydroepiandrosterone (DHEA) and cortisol; and the immunological parameters of lymphocyte proliferation to phytohemagglutinin (PHA), natural killer (NK) cell activity, CD4+ and CD8+/CD57+ lymphocyte levels, and selected type 1 and type 2 cytokine levels in individuals infected with the human immunodeficiency virus (HIV). These parameters were chosen because of their interrelationships within the PNI framework and the potential of the interrelationships to affect positively neuroendocrine and immune function in individuals living with HIV disease. HT was chosen because of its potential to enhance immune function through its ability to enhance well-being. This study will add to a growing body of scientific investigations of PNI and energy-based therapies.

Purpose

The purpose of this study was to ascertain the effects of HT on selected PNI parameters in HIV-infected participants. It was hypothesized that HT would increase participant well-being, which subsequently would increase both serum serotonin and salivary DHEA, decrease salivary cortisol, and ultimately enhance immune function. Specific research hypotheses were that HT would (1) enhance well-being, (2) increase levels of serum serotonin and DHEA, (3) decrease levels of salivary cortisol, and (4) enhance immune function in persons with HIV disease. Ultimately, HT may be beneficial as part of a comprehensive, integrative program combining allopathic and complementary therapies to improve the quality of life and survival of persons living with HIV disease. However, decision-making regarding clinical applicability of energy therapies requires further scientific evaluation.

Conceptual Framework

The conceptual framework for this study is presented schematically in Figure 1.

Human beings are conceptualized as energetic beings comprised of contiguous, continually

interacting human and environmental energy fields. Energy-based therapies such as HT

allow practitioners to assess and correct imbalances in the energy field to promote health

and well-being. Because PNI encompasses a holistic view of mind-body interactions, it

provides a framework for investigating therapies such as HT that potentially can impact

the interactions among psychological factors such as well-being and neuroendocrine and

immune function.

Healing Touch

Brennan (1987) provided a comprehensive history of energetic healing in Hands of

Light: A Guide to Healing through the Human Energy Field. Throughout history, in both

the east and west, are descriptions of a universal energy pervading all living things. In

traditional Chinese medicine, it is known as chi. In Ayurvedic medicine, it is called prana.

This energy was first described in the west around 500 BC by the Pythagoreans. This vital

energy manifests itself in human beings as a human energy field (HEF). Since the 12th

century, western science, through various techniques including photographic and

electromagnetic procedures, has accumulated evidence to support the presence of a HEF.

Based on observations over the centuries, a theoretical model has been developed

that describes the energy field as being composed of seven layers. The seven layers are

connected to the physical body, to each other, and to universal energy by chakras or

energy vortexes. Disturbances or imbalances in the HEF can be assessed and altered

intentionally through the chakras. As mentioned, each chakra is believed to correspond to

a specific endocrine gland and particular area of the body. A diagram of the seven major chakras and their theorized corresponding endocrine glands and body regions is provided in Appendix A. Because the chakras are believed to vitalize the body, they are directly related to health and illness. According to Moore (1997), "the basic premise of most energy medicine models is that dysfunctions occurring with the chakras translate down into the physiological level" (p. 47).

HT is an energy-based therapy developed in the 1980's by Janet Mentgen, based on earlier work by Kunz and Krieger (Brennan, 1987). The underlying premise of HT is consistent with ancient descriptions of the body as a complex energy system whose physiological functions are influenced by the flow of that energy. Through the use of HT, it is postulated that a recipient's energy flow can be assessed and balanced. The particular HT technique used in this trial was the chakra connection, which is used to balance and connect the major energy centers or chakras. The purpose of the chakra connection is to restore balance in the human energy field to promote psychological and physiological health. Eisenberg (1993), a western-trained physician and expert in traditional Chinese medicine, stated that "energy medicine" is in no way inferior to synthetic drugs and other biomedical therapies, it simply uses a different approach to health and illness. However, well-designed trials are needed to assess the effects of energy-based therapies.

Well-being

For the purpose of this study well-being was a measure of the potential effects of HT as well as the primary link between HT and PNI. Well-being has been defined as "the state of being generally healthy, happy, or prosperous" (Riverside Webster's II Dictionary, 1996, p. 769). According to Bradburn (1969), well-being is conceptualized as having an

affective-emotional component as well as a cognitive-judgmental component. Basically, an individual experiences positive well-being when positively perceived emotions outweigh negatively perceived emotions, and vice versa. It is not the absolute amount of positive or negative emotion that determines the affective-emotional aspect of well-being, but the balance between the two. The cognitive-judgmental component reflects the individual's satisfaction with life. Thus, subjective well-being is the individual's perception of the balance of positive and negative emotions as well as satisfaction with his or her goals in life and the perceived potential to achieve these goals.

Consistent with Bradburn's conception of well-being, Dossey and colleagues (1995) defined well-being as a process of increasing awareness of reaching human potentials. According to the Rogerian energetic framework, well-being can be conceptualized in terms of human field image (HFI). Generally, HFI is an individual perception of the infinite wholeness of the human field (Johnston, 1994). Johnston defined HFI as "one manifestation of the human and environmental patterning process, which may be expressed as a perception of one's potential and an awareness of one's integrality" (p. 8). Perceived potential encompasses concepts related to the perception of the presence or absence of boundaries, while integrality represents manifestations of the perceived human-environmental mutual process. Thus, well-being can be conceptualized as an individual perception comprised of physical, psychological, and energetic dimensions encompassing overall health, positive and negative emotions, as well as the recognized potential for achieving and maintaining wellness and balance in life.

Immune Function

The functioning of the immune system is orchestrated by a variety of cells and cellular products. Immune cells are collectively identified as leukocytes or white blood cells (WBC's). WBC's are divided into three main categories: lymphocytes, monocytes, and granulocytes. Functional differences exist among these broad categories with further distinctions delineated among lymphocyte subpopulations. Lymphocytes are divided into B cells, T-helper cells, T-suppressor cells, and NK cells. B cells protect against bacterial infections and produce antibodies. T-helper cells stimulate immunological activities, and T-suppressor cells down-regulate immune responses. NK cells are non-specific cytotoxic or cell-killing cells. Unlike other cytotoxic lymphocytes, they do not require prior sensitization to induce a cytotoxic response. They provide antiviral and antitumor protection. Because there are so many different cells performing so many different processes, immune function can be assessed using a variety of approaches. Enumerative measures assess the number and/or percentage of particular cells. Functional assays assess processes such as lymphocyte proliferative response to antigens, specific cytotoxic activities, and the ability to generate humoral regulatory substances such as antibodies and cytokines (Weisse, 1992).

HIV Disease

According to Folkman (1993), the psychosocial effects of HIV disease cannot be understood without some basic understanding of HIV disease. HIV is transmitted through interpersonal sexual contact with an infected individual, exposure to contaminated blood or blood products, and perinatally from an infected mother to her infant. The physical course of HIV varies widely. Within several weeks of infection, individuals can develop a

self-limited acute illness that is similar to mononucleosis, with fever, sore throat, malaise, skin rash, headache, and lymphadenopathy. Following resolution of this illness, there is usually an extended incubation or "latent" period, which varies in length from 1 to 10 years. During this latent phase, individuals are relatively healthy with periodic symptoms such as lymphadenopathy, fatigue, low-grade fevers, and other non-specific symptoms. Some individuals have no physical symptoms or laboratory abnormalities during this time.

The next phase is marked by minor infections such as oral candidiasis, herpes zoster, and recurrent herpes simplex outbreaks. Other non-specific symptoms that can occur during this time include fevers, night sweats, weight loss, diarrhea, and skin rashes. As the disease progresses and cellular immunity becomes more impaired, opportunistic infections, tumors, neurological disorders, and more severe weight loss (>10% of ideal body weight) develop. The aforementioned non-specific symptoms usually continue. The diagnosis of AIDS is established with the occurrence of any of the AIDS-indicator conditions defined by the Centers for Disease Control and Prevention (CDCP) such as pneumocystis pneumonia, wasting syndrome, and encephalopathy. HIV medication regimens are focused on inhibiting viral reproduction, maximizing immune function, and preventing concurrent infections. Because of the extended asymptomatic phase and the stabilizing effects of medications, HIV is now considered a chronic disease (Folkman, 1993).

PNI

PNI is the study of the complex interactions among behavior and the neuroendocrine and immune systems. It is considered a holistic framework because it encompasses these interactions, which were previously conceptualized as separate and

isolated entities. The field of PNI grew from the realization that the immune system does not function autonomously. Currently the immune system is perceived as a large sensory organ providing indirect feedback to the central nervous system (CNS) through messenger chemicals such as cytokines. The CNS is physically and systemically connected to the immune system by the autonomic nervous system and neuroendocrine outflow from the pituitary gland. Sympathetic neurons innervate immune organs including the thymus, bone marrow, spleen, and lymphatic system. These nerve fibers communicate directly with immune cells such as lymphocytes. Lymphocytes express soluble mediators for CNS and neuroendocrine substances, such as hormones and neurotransmitters, and have specific receptors for such mediators on cell membrane surfaces. The immune system is also influenced by neuroendocrine outflow from the pituitary. Following the release of stimulating substances from the pituitary, the adrenal cortex produces two steroid hormones that affect immune function: cortisol and DHEA (Ader, Cohen, & Felten, 1995).

Cortisol is the major glucocorticoid produced by humans and potentially the most important steroid hormone influencing immune function within the context of PNI. According to Reichlin (1993), cortisol, when produced in excess, has the potential to interfere with virtually all components of the immune response. Cortisol reduces lymphocyte numbers as well as cellular function (Hillhouse, Kiecolt-Glaser & Glaser, 1991; O'Leary, 1990; Stein & Miller, 1993). Its immunosuppressive effects are often related to regulatory interference with cytokines (Clerici, Bevilacqua, Vago, Villa, & Norbiato, 1994).

DHEA is produced in the adrenal cortex and is the most abundant steroid hormone in the body. Research exploring the physiological role of DHEA confirms its major regulatory function in the immune system (Regelson, Loria, & Kalimi, 1994). For example, Khorram, Vu, and Yen (1997) found that immune function improved significantly following oral supplementation of DHEA in aged men. Increased numbers of monocytes, NK cells, and B-lymphocytes, as well as an increase in lymphocyte proliferation evidenced enhanced immune function.

Psychological modulation of immune function has been investigated in two primary areas: classical conditioning and the impact of stress. Ader and Cohen (1975, 1993) paired a saccharin solution with cyclophosphamide (a chemotherapy agent) and demonstrated a conditioning effect on the immune system in the form of significant immunosuppression when the saccharin solution was given without the immunosuppressive drug. This discovery was a pivotal finding in the development of the field of PNI. Solvason, Ghanta, and Hiramoto (1988) also demonstrated conditioned immune enhancement.

Stressors activate the sympathetic nervous system as well as the hypothalamic-pituitary-adrenal axis, thereby potentially impacting immunity. Although Selye (1956) originally proposed a model of nonspecific responses to various stressors, it is now accepted that different types and patterns of stressors can produce different patterns of autonomic responses (Mason, 1971). Additionally, individual factors such as personality, coping styles, and affective states can modulate physiological responses (Friedman & Booth-Kewley, 1987; Chesney & Rosenman, 1983; Herbert & Cohen, 1993).

There is increasing evidence that immune processes occur within a neuroendocrine

environment that is "sensitive to the influence of the individual's perception of and response to events in the external world" (Ader, Cohen, & Felton, 1995, p.100). PNI provides a framework for conceptualizing and investigating the means by which psychosocial factors and affective states can influence the development and progression of immunological diseases.

PNI in HIV Disease

To date, much of the research done in the field of PNI has focused on individuals with impaired immune function, such as those individuals living with HIV disease, because even subtle changes in the neuroendocrine and immune systems of these individuals are potentially helpful in maintaining adequate immune function and health. Cellular immune reactions are under the regulation of two categories of lymphocytes, T-helper (CD4+) and T-suppressor (CD8+) cells. The relative numbers and function of these lymphocytes influence the strength and persistence of immune responses. HIV primarily infects the CD4+ helper/inducer lymphocyte, a key cell type in regulation of both cell-mediated and humoral immune responses. Ultimately, HIV destroys CD4+ cells; measurable reductions in CD4+ lymphocyte counts occur when cell destruction exceeds cell replication. This decline in CD4+ lymphocytes correlates with HIV disease progression. With disease progression, in addition to T-lymphocyte functional impairment, NK cell function is also impaired (Brenner, Dascal, Margolese, & Wainberg, 1989; Clerici et al., 1989).

NK cells are part of the host's natural immunity to HIV-associated disorders and opportunistic infections. In vivo, NK cells play a vital role in fighting infections by producing cytokines, such as tumor necrosis factor (TNF)-alpha and interferon (IFN)-gamma, even before T-cell activation occurs. Generally, there is no significant enumerative

change in NK cells in HIV disease. However, NK cell function may be of major prognostic significance in AIDS pathogenesis. Normally, NK cells spontaneously lyse virally infected and cancerous cells. However, NK cells become functionally defective as HIV disease progresses and the cause of this dysfunction remains unknown (Brenner, Dascal, Margolese, & Wainberg, 1989; Chehimi et al., 1992; Sirianni, Tagliaferri, & Aiuti, 1990).

According to Clerici and Shearer (1993, 1994), an immune system imbalance occurs in HIV disease that further weakens the immune system and accelerates the progression to AIDS. They proposed a shift from type 1 to type 2 cytokine regulation as a critical step in the progression of HIV infection. Cytokines may be an immunologic marker of HIV disease progression. Increased levels of soluble cytokine receptors in HIV-infected individuals are associated with a chronic state of cellular activation that is an important part of the pathogenesis of HIV disease. According to Poli and Fauci (1996), this ongoing immune activation likely contributes to a state of persistent HIV replication, underlying a vicious cycle of activation and virus replication that fosters the progression of HIV disease.

Cytokines are proteins that function through intercellular receptor binding. They regulate immune system functioning including cellular and humoral immune responses. Cytokines are known to be behaviorally, endocrinologically, immunologically, and electrophysiologically active (Ader, Cohen, & Felton, 1995). The cellular and humoral arms of the immune system tend to counteract each other by cytokine regulation. Evidence suggests cytokine response patterns are involved in immunomodulation (Mosmann & Sad, 1996). Generally, a type 1 cytokine pattern (including interleukin-1[IL-1], IL-2, IL-12, IFN-gamma, and TNF-alpha) enhances cellular immunity, while a type 2 pattern (including

IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13) diminishes cellular immunity and enhances humoral immunity. Type 1 cytokines stimulate effector responses to viral infection and other intracellular pathogens through activation of NK cells and cytotoxic lymphocytes. Type 2 cytokines support effector responses to bacterial and parasitic infections and mediate allergic responses by promoting antibody production. Cross-regulation exists between type 1 and type 2 cytokine responses. For example, IFN-gamma and IL-12 functionally down-regulate type 2 responses and IL-4 and IL-10 functionally down-regulate type 1 responses. Conversely, inhibition of IFN-gamma and IL-12 will augment type 2 responses and inhibition of IL-4 and IL-10 will enhance type 1 responses (Shearer & Clerici, 1992; Clerici & Shearer, 1993; Levy, 1993; Kuby, 1994). While these mechanisms are generally exhibited, the exact role of cytokines remains a complex issue. Depending on the cytokine milieu and/or functional status of an infected cell, IFN-gamma, IL-4, and IL-10 can act as positive or negative modulators (Poli & Fauci, 1996). Shearer and Clerici (1996) acknowledged that their theory does not take into account the "interaction of immunoregulatory cytokines produced by the many different cell types operating in a dynamic and open system" (p. 230).

The progressive dysfunction of the immune system in HIV disease ultimately results in increased susceptibility to opportunistic infections and the clinical syndrome of AIDS. However, the clinical course of HIV is highly variable with or without treatment. The variability in the clinical and biological course of HIV may be due solely to properties of the virus itself, although it is most likely that environmental and/or host cofactors also influence disease progression (Kemeny, 1994). Although the relationships among behavior

and mood, immune function, and HIV disease progression are not yet clear, there is reason to believe these relationships exist (Schneiderman, 1994).

In a review of stressful events, psychological responses, and progression of HIV disease, Kemeny (1994) cited multiple physiological and psychological cofactors for HIV disease progression, including substance abuse, malnutrition, sexually transmitted diseases, the presence of other viral infections, and negative affective states such as dysphoria, bereavement, fatalistic thinking, and hopelessness. Currently, there is little empirical support for the relationship between psychological well-being and immune function. However, stress and coping effectiveness are considered cofactors for HIV disease progression and there is significant empirical support for a relationship between stress and psychological distress, or the individual's reaction to stress, and HIV disease progression (McCain & Zeller, 1996). Similar mechanisms may be responsible for the relationship between dysphoric or negative affective states and immunosuppression (Herbert & Cohen, 1993). Additionally, the relationship between stress and immune function is mediated, in part, by an individual's perception of potentially stressful events. Similarly, an individual's mood could potentially mediate immune function. Whereas a negative affective state may diminish immune function, a positive affective state may enhance immune function. In a comprehensive review of studies involving PNI and HIV disease, McCain and Zeller (1996) concluded that because of the paucity of studies of well-being as well as design and validity problems, there is currently little empirical support for relationships between well-being and immunity. They proposed two research priorities: (a) investigating the effectiveness of nursing interventions in HIV disease, and (b) identification of biobehavioral factors and testing interventions that foster immunocompetence. This

clinical trial contributes to the developing knowledge base of the effectiveness of the biobehavioral intervention of HT in fostering immunocompetence in individuals living with HIV disease. It was proposed that HT may enhance well-being because of its potential to elicit the relaxation response and decrease anxiety and physical discomfort. It is conceivable that interventions, such as HT, that enhance well-being and possibly neurally mediated immune function, may enhance quality of life as well as retard HIV disease progression. This trial was needed to investigate the host cofactor of well-being, a global indicator of an individual's perception of their day-to-day life and long-term aspirations, and its possible effects on the neuroendocrine environment and immune function in individuals living with HIV disease.

In summary, PNI provides a holistic framework for examining interactions among psychological states and the neuroendocrine and immune systems. This framework is particularly applicable in immunologically mediated diseases such as HIV disease. PNI research in HIV disease has focused primarily on the impact of stress and negative affective states on disease progression, while the potential impact of positive affect remains largely unexplored. HT and other energy therapies are theorized to focus on healing at the quantum and electromagnetic levels in individuals. These therapies are also associated with the elicitation of the relaxation response. Generally, these therapies have the potential to enhance well-being in a variety of ways, although the exact mechanisms of action are not yet known. In this research, PNI serves as an organizing paradigm for investigating the effects of HT on well-being in individuals living with HIV disease. It was specifically proposed that HT had the potential to improve well-being, thereby eliciting favorable changes in the neuroendocrine environment and ultimately enhancing immune

function. Despite the complexity of investigating immune function in the presence of somewhat unpredictable and often inadequately understood immune dysfunction, if even subtle effects of HT on neuroendocrine and immune function are detected, their impact may be clinically significant in individuals with impaired immune function. This trial sought to examine the effects of HT on well-being and ultimately immune function, but because it was not a longitudinal study, it provided only theoretical conclusions about health outcomes.

Significance

PNI provides a comprehensive conceptual framework for investigating the relationship between the mind and the body as well as interventions that may influence this relationship. Research indicates that stress and its correlate, psychological distress, can alter immune function, thereby influencing disease susceptibility (McCain & Smith, 1994). However, investigations into the clinical applicability of mind-body interventions for promoting health and treating disease are limited (Zeller, McCain, & Swanson, 1996). The research that does exist focuses on the impact of distress or negative affect, while the effects of positive affect or subjective well-being have been largely unexplored. It is theoretically sound to propose that if negative affect can impair immune function, then positive affect may enhance immune function. In individuals whose immune function is impaired, as is the case in individuals living with HIV disease, even subtle changes in immune function could affect health. This clinical trial provided valuable insights into the the effect of HT using a PNI paradigm.
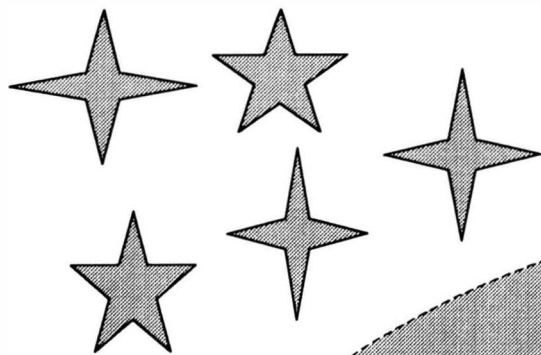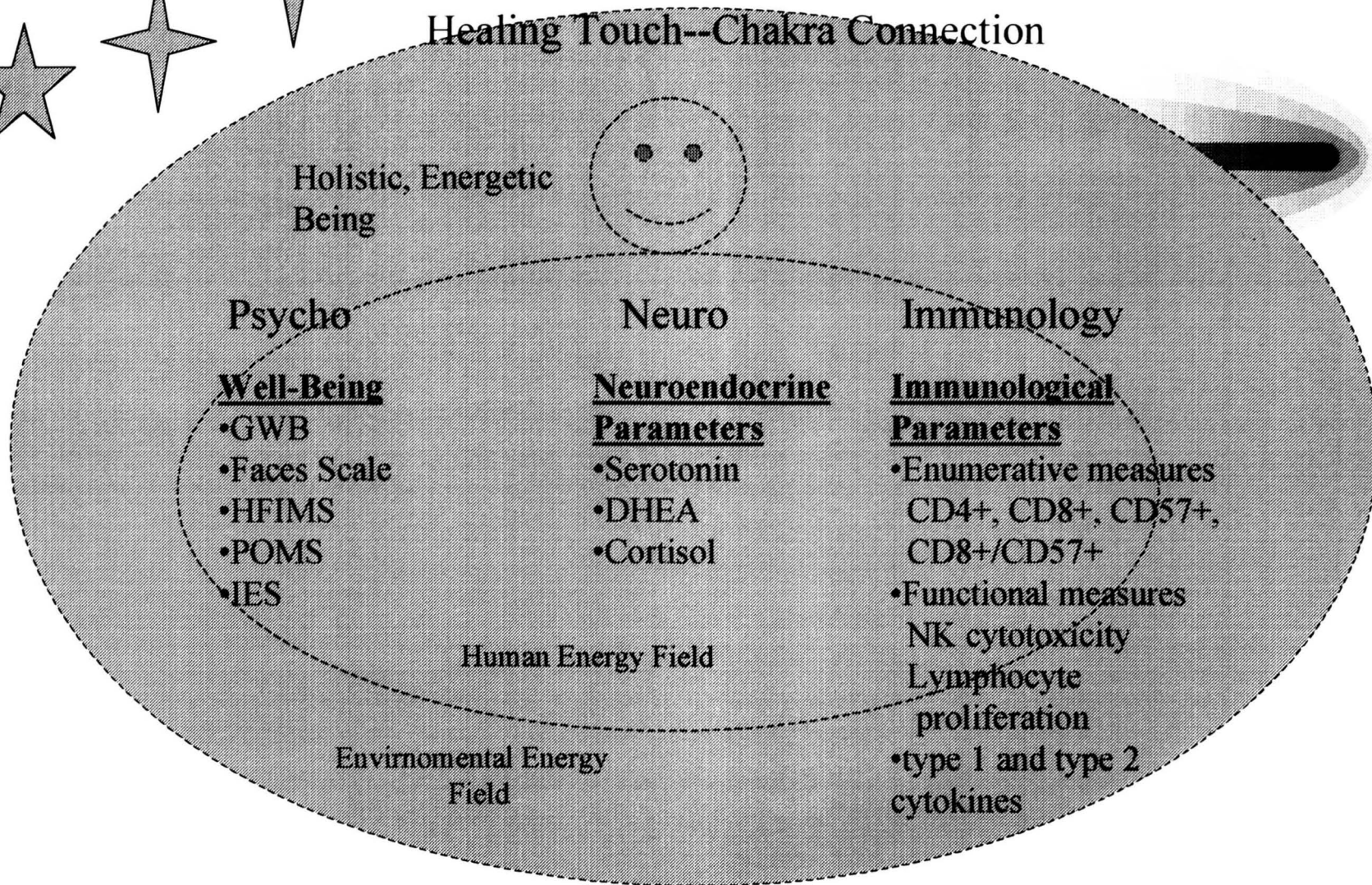
Figure 1. Conceptual Framework: Psychoneuroimmunology and Healing Touch in HIV Disease

Chapter 2

Review of Research

The components of the research review are structured according to the purpose of this clinical trial, the investigation of the effects of HT on well-being , the neuroendocrine environment, and immune function in individuals living with HIV disease. The review is representative of the applicable research that exists in the areas of energy therapies, well-being, the interactions among the neuroendocrine and immune systems, immune dysfunction in HIV disease, and the field of PNI in HIV disease.

Healing Touch

Only two studies evaluating the effects of HT were found in peer reviewed journals. In an anecdotal case study, HT was shown to facilitate healing of a cesarean wound infection (Wetzel, 1993). HT was performed every other day for 12 days (from postoperative day 8 through 19), then on postoperative days 25, 31, and 47. Generally, the treatment consisted of magnetic unruffling followed by the conscious direction of energy into the wound. This patient also received standard wound care, including oral antibiotics and wound irrigation and dressing changes three times a day while the open wound healed by second intention. Other patients who had wound infections during the same time period as the patient in the case study had taken 9 to 16 weeks to heal.

Wetzel reported the patient treated with HT had a similar wound but was fully healed in 6 weeks. However, the lack of research controls for this study obviated meaningful comparisons.

In the other study, HT was shown to decrease postoperative pain. Silva (1996) assessed the effects of HT on postoperative pain, relaxation levels, and physiological functioning in a sample of 60 women who had abdominal hysterectomies. Participants were assigned randomly to one of three groups: HT, back massage, or no treatment. Each group consisted of 20 participants. The treatment group received a 20-minute HT intervention while one control group received a 20-minute back massage and the other control group received standard postoperative care on the day of surgery and 24 and 48 hours after surgery. A nursing assessment, including vital signs, and activity level as well as lung, gastrointestinal, urinary, and motor function, was performed before and after each session and on the third postoperative day. The amount of self-administered narcotic analgesia and the number of medications and treatments to stimulate bowel function were recorded daily. Data were analyzed using repeated measures analysis of variance and analysis of covariance. Participants who received HT experienced a higher level of recovery as evidenced by more rapidly improved lung and gastrointestinal function as well as higher activity levels when compared to the back massage and control groups. The HT group also experienced statistically significant reductions in systolic and diastolic blood pressure and pulse rates. Additionally, the HT group received significantly less narcotic analgesia and fewer bowel treatments compared to the other groups.

In a doctoral dissertation published in Dissertation Abstracts International, Slater (1996) investigated the effects of HT on chronic non-malignant abdominal pain in 23 participants who had a history of abdominal surgery. Each participant received three different treatments on separate days: HT administered by experienced practitioners, HT administered by inexperienced or "naïve" practitioners, and an interview. The order of the treatments was randomly assigned. The treatments given by the experienced and inexperienced practitioners were identical, consisting of the HT techniques of magnetic unruffling and wound sealing. The interview was used as a placebo control to assess whether HT elicited a greater response than did a nurse being and talking with a patient in pain. Pain perception was measured before and after treatments using the McGill-Melzack Pain Questionnaire (MMPQ). Additionally, qualitative data exploring the practitioners' and recipients' experiences were collected then analyzed using content analysis. There were no significant differences in pain perception as measured by the MMPQ following either of the HT sessions. Inexperienced practitioners experienced more physical discomfort during sessions than did the experienced providers. Interestingly, the recipients preferred the inexperienced practitioners because the recipients experienced more nausea, headaches, dizziness, and drowsiness with the experienced practitioners. However, participants subjectively reported greater pain relief and relaxation following treatments with experienced HT practitioners despite the increase in other symptomatology. The author proposed this may indicate that the MMPQ differentiates between dimensions of pain, but that individuals experiencing pain may evaluate their pain based on criteria other than pain sensations. In this investigation, HT did not decrease postoperative pain

significantly. The effect of the therapeutic interview on pain levels was not mentioned in the abstract. The small sample size may have contributed to the lack of statistical significance.

Healing Touch International publishes an annual survey of HT research containing information on upcoming, ongoing, and completed research. The survey includes abstracts of the completed HT research. Several of these studies are applicable to this research and therefore are included in this review of the literature. Some of these studies were recently completed and publications are in process. However, the majority of them are not being published in professional journals. Although the studies provide some potentially valuable information about the experience and effects of HT, they generally lack adequate methodological rigor.

DuBrey (1998) explored perceived effectiveness of HT treatments in a convenience sample of 25 individuals visiting a rural wellness center. The participants were ambulatory patients visiting a community-based wellness center; however their health status was not mentioned in the abstract. Following a single HT session, individuals were asked to rate pain perception, stress perception, and emotional well-being on a 1 to 10 scale, with 1 being the least change and 10 being the greatest. Participants were asked to document the lasting effectiveness of treatment at 1 to 3 days, 4 to 7 days, 1 to 2 weeks, and greater than 2 weeks. None of the participants experienced an increase in pain or stress or a decrease in well-being following treatment. A total of 92% ($\underline{n}$=23) experienced decreased stress following HT, 68% ($\underline{n}$=17) experienced decreased pain, and 88% ($\underline{n}$=22) experienced an increase in well-being. The reduction in stress levels persisted for up to 3 days in 36% of participants, up to 7 days in 20%, up to 2 weeks in 11%, and greater than

2 weeks in 28% of participants. Pain reduction was sustained for up to 3 days in 33% of participants following healing touch, up to 7 days in 28%, up to 2 weeks in 11%, and greater than 2 weeks in 28% of the participants. Increased levels of emotional well-being persisted for up to 3 days in 12% of the participants, up to 7 days in 32%, up to 2 weeks in 16%, and greater than 2 weeks in 40% of participants following HT. The researcher concluded that 88% of individuals reported a significant increase in their feelings of emotional well-being and 40% of those individuals experienced increased well-being that persisted for more than 2 weeks. Caution is required when interpreting the findings of this study because there was no control group and all measures were highly subjective and vulnerable to reactivity.

One investigator examined the effects of HT on depression. Leb (1998) recruited 30 individuals with moderate to severe depression, as measured by the Beck Depression Inventory, then randomized them into treatment and no treatment control groups. The treatment group received HT twice a week for 3 weeks. They received the same treatment each week, consisting of centering, chakra spread (to open the energy field), magnetic unruffling (to clear any debris or imbalance in the field), modified mind clearing (to balance neurochemicals), seventh chakra spread (to clear the individual/universal connection), and terminating the session. The participants who received HT were significantly less depressed at the end of the 3-week intervention as compared to the control group who received no HT treatment. Depression levels were assessed one month later and the treatment group continued to demonstrate lower levels of depression compared to baseline. Information about the equivalence of groups at baseline was not addressed. No alternate explanations were offered for the improvement in the treatment

group such as social support, medications, or psychotherapy. Additionally, these variables were not addressed as potential confounders.

One qualitative investigator explored the subjective experience of the chakra connection, the HT technique proposed in this trial. Moreland (1998), in a phenomenological inquiry, asked six women who were undergoing intravenous chemotherapy for breast cancer to describe the experience of receiving HT with as much detail as possible. Three primary themes were identified. The experience was perceived as (a) caring expressed as a partnership, a nurturing act, and as self-care; (b) creating altered consciousness of the passage of time, the surrounding environment, of thought, and of the presence of the practitioner; and (c) a holistic experience involving physical, mental/emotional, and spiritual dimensions. The author concluded that HT for this group of participants was a "holistic, caring, and variable experience which altered their perception of self, time, and their surrounding environment in a positive way. This helped them 'get through' the experience of the chemotherapy" (p. 11). This was a well-designed and conducted phenomenological inquiry providing insight into the experience of receiving HT, but because of its qualitative design the findings cannot be generalized to other practitioners and recipients.

Wilkinson (1998) is currently conducting a three-phase study focused on understanding the effects of energetic healing. Phase 1 of the research was a qualitative exploration into the experience of receiving HT and has been completed. Phases 2 and 3 are in progress. Phase 2 is quantitative and involves laboratory analysis of salivary IgA concentrations before and after HT. Phase 3 will involve integrating Phases 1 and 2. In Phase 1, the researcher interviewed 12 HT practitioners and 7 HT recipients about the

experience of HT. The inquiry involved details about the experience, whether or not HT promoted health and personal growth, and from the recipients' perspectives, which elements of HT were perceived to be the most effective. Following content analysis, five themes were identified: changes, relaxation, an awareness of process, practitioner deliberateness, and heightened holistic awareness. All recipients except one reported positive changes following HT. The perceptions of the recipient whose experiences were unfavorable were not described in the Healing Touch International report. Relaxation, physical touch, and energy exchange were the answers given most frequently when recipients were asked which elements of HT they found most beneficial. Details about the practitioners' responses were not included in the research abstract. Once again, information about the experience of receiving HT is provided which may infuse meaning when interpreting the psychophysiological responses to HT. However, data generation and analysis procedures and issues related to rigor and trustworthiness were not addressed in the abstract.

Included in the HT survey was a brief report regarding data informally collected by Lorene spanning greater than 300 hours of work with HIV-seropositive clients in her capacity as a volunteer at the Holistic AIDS Response Program at the University of California at San Diego. Because the sample was comprised of HIV-seropositive individuals treated with the chakra connection, this research is included here as reported through personal communication with the researcher. During 1-hour HT sessions, the researcher performed magnetic unruffling, chakra connection, and a modified brain balance technique. Clients were typically dealing with symptoms related to pain or agitation or both. In clients experiencing pain, pre- and post-treatment evaluations of pain

were completed using a 1-10 scale, with 1 being "minimal pain" and 10 being "the worst pain ever." Responses in the 8-9 range consistently dropped to 0 by the end of the HT session. To assess agitation, clients' verbal responses were assessed before and after HT. Subjective reports consistently demonstrated considerable agitation or anxiety pre-treatment and feeling calm and relaxed post-treatment. Lorene stated that HT is part of routine HIV-related care at the holistic center because the outcomes are so positive (Jo Lorene, personal communication, November 13, 1998). These data provide interesting anecdotal information about the effects of HT in individuals living with HIV disease. However, it does not provide sufficiently rigorous scientific information about the effects of HT in HIV disease.

<u>Therapeutic Touch Research</u>

Because there are limited peer-reviewed HT publications and HT and therapeutic touch (TT) are related energy-based therapies, a review of TT research is also included. Krieger and Kunz, a nurse and a healer, developed TT in the 1970's. Its origins are based on the ancient technique of laying on of hands, traditional eastern medicine, as well as quantum physics (The Burton Goldberg Group, 1995; Castleman, 1996). Generally, the practitioner does not physically touch the recipient during TT. The hands are placed 2 to 6 inches away from the body. HT is a comprehensive framework of energy-based therapies which subsumes the technique of TT. HT was developed after the introduction of TT into nursing practice and literature. It shares the same theoretical basis but is comprised of a wider variety of techniques (involving both physical touch as well as working 2 to 6 inches away from the body) specific to particular energy imbalances or physical illnesses and involves a longer, more complex certification process. According to Slater (1995), who

developed a theory of energetic healing based on physics, energetic healing is healing that occurs at the quantum and electromagnetic levels of an individual. According to this theory, all energy therapies are based in the laws of physics and, fundamentally, all are varying techniques that elicit similar effects.

Therapeutic touch and the relaxation response. TT has been shown to induce a generalized relaxation state. As described by Krieger and colleagues (1979), this response included dilation of the vessels of the skin, decreased vocal pitch, and a subjective feeling of tranquility in clients undergoing TT. The most interesting finding in this small experiment were the electroencephalogram (EEG) findings. Generally, when the eyes are closed and a person is in a calm state of mind, an alpha state exists. A normal state of wakeful awareness is a beta state. The participants exhibited alpha wave activity on EEG even though their eyes were open. When questioned, they expressed a sense of well-being. Despite the intriguing results of this report, there were only three participants and no form of scientific control was applied.

Based on the premise that a TT encounter affects both the recipient and the practitioner, a more recent study evaluated the presence of the relaxation response in nurses performing TT (Sies, 1994). The researcher recruited eight nurses who had been practicing TT for at least one year and measured peripheral skin temperature while they performed TT for at least 15 minutes. Sies found that 50% of the practitioners demonstrated a relaxation response as evidenced by increased peripheral skin temperature. The personal practice of meditation or other relaxing therapies was not assessed or controlled in the practitioners. Furthermore, half of the practitioners did not demonstrate a significant relaxation response.

TT and hemoglobin. Extensive work has been done on the physiological and psychological effects of TT since it was introduced by Krieger in 1974 (Quinn, 1988). Krieger (1975) demonstrated a significant increase in hemoglobin levels in hospitalized adults following TT. A convenience sample of 64 patients was treated with either TT or routine nursing care. There were no significant differences among baseline hemoglobin levels. Despite a reported increase in mean hemoglobin levels, rigor was lacking in this early trial. There were no operational definitions or randomization procedures and hemoglobin values were not included in the report.

TT and pain. Several trials have shown TT to decrease pain. In a quasi-experimental trial, Keller and Bzdek (1986) investigated the effects of TT on tension headache pain. Based on the premise that TT reduces anxiety and given there is an anxiety component in tension headaches, a sample of 60 healthy participants with tension headaches was randomly assigned to the TT intervention or a mimic TT control group. Each participant received a 5-minute intervention. The researchers did TT sessions and data collection. In the TT group, the researcher centered and entered a quiet meditative state, making a conscious intent to help the recipient. In the mimic TT control group, there was no attempt to center or reach a meditative state. The researcher performed the same movements as with the TT group while focusing on the mental task of subtracting from 100 by 7s. Pain levels were measured immediately prior to the intervention and 5 minutes and 4 hours after the intervention using three subscales of the McGill-Melzack Pain Questionnaire. A Wilcoxon signed-rank test for differences revealed that 90% of the participants exposed to TT reported a sustained reduction in headache pain. The TT group experienced twice the amount of pain relief at 4 hours when compared to the control

group. The control group also experienced some headache pain relief, perhaps validating potential placebo or Hawthorne effects. This study included an adequate sample size and randomization to groups. However, statistical analysis was weak and the study design did not address potential covariates. Additionally, the researcher administered the treatments as well as the pain questionnaires, allowing for significant practitioner-participant effects. Finally, even though the practitioner consciously attempted to block any intention to help or direct energy during the mimic sessions, the effect of a caring presence cannot be excluded, especially in light of a decrease in headache pain in the control group. To this researcher, the TT mimic or sham control is an inadequate control condition, primarily because of the presence of a caring individual. The majority of the individuals performing the mimic sessions are nurses and although they are not trained in TT, they represent caring presence, rendering attribution of any detectable effects to TT difficult. Assessing the effects of energy therapies is at best complicated, even when controlling for confounding variables that potentially affect the dependent variable of interest. Additionally, the mechanism of action of energy therapies remains unknown. If it is actual energy exchange or modulation, this cannot currently be measured adequately. A no-treatment control group is a better alternative because it removes the possibility of effects related to therapeutic human contact.

Meehan (1993) studied the effects of TT on postoperative pain in 108 individuals following major elective abdominal or pelvic surgery. Individuals were randomized into three groups: TT intervention, mimic TT intervention (MTT), and the standard intervention (SI) of analgesic medication as needed (PRN). Pain levels were measured using the Pain Visual Analogue Scale (VAS) before and one hour after the assigned

intervention. The author identified the VAS as a widely recognized, valid and reliable tool for measuring acute pain. Validity of the VAS was assessed in this study by correlating participants' verbal pain intensity descriptors with their VAS scores. The descriptors were: "no pain," "mild pain," "moderate pain," "severe pain," and "pain as bad as can be." The overall descriptor-VAS correlation was .72. If individuals receiving TT or MTT requested pain medication, they were assigned a post-intervention pain score equal to their pre-intervention score for the purpose of statistical analysis. Using analysis of covariance, the SI group was found to have statistically significant reductions in pain. The TT group also experienced a decrease in pain but not equal to the level of reduction in the SI group. The MTT group did not experience any decrease in pain following their intervention. The participants who received TT did wait a significantly longer period of time in requesting additional PRN analgesia when compared with the MTT group. The authors concluded that TT is a useful adjunct to PRN analgesia for postoperative pain but should not be relied on exclusively for effective pain control. Adequate sample size, randomization procedures, consideration of covariates, and the researcher not playing the role of practitioner were strengths of this clinical trial. The use of a visual analogue scale and the use of a mimic TT control group were weaknesses of the study.

Peck (1997) investigated the effects of TT on pain and distress related to degenerative arthritis (rheumatoid or osteoarthritis) in 82 elders. Participants served as their own controls for a 4-week baseline period while receiving routine arthritis care consisting of medications, heat or cold applications, prescribed rest or exercise, physical therapy, chiropractic therapy, massage, and steroid injections. Following the 4-week baseline period, the participants were assigned randomly to receive one TT or progressive

muscle relaxation (PMR) session weekly for 6 weeks. Additionally, participants were

assigned randomly to practitioners to "control for the differences in personality and

interaction style of the practitioners" (p. 12). The author chose PMR as the comparison to

avoid the limitations associated with TT sham or mimic controls. The limitations of sham

therapy identified were nurses' anxiety related to consciously withholding a therapeutic

treatment and a placebo effect transmitted by the nurse during a sham treatment. A total of

45 participants received TT while 37 received PMR. Two visual analogue scales were

used to measure pain and distress before and after each session. The scales consisted of

10-centimeter (cm) vertical lines, with the pain scale ranging from "no pain" to "worst

pain imaginable" and the distress scale ranging from "doesn't bother me" to "unbearable."

There were statistically significant reductions in pain and distress in both groups, with the

greatest reductions being in the PMR group. Additionally, there were clinically significant

improvements in the participants' physical abilities during the study. Participants reported

the ability to perform activities they had not been able to perform as well as increased ease

in performing routine daily activities. TT was not as effective as PMR in decreasing

arthritis pain, perhaps because of the therapeutic use of the muscles in PMR or because

TT does not elicit as deep a relaxation response. This study included an adequate sample

size, randomization procedures, and a researcher who did not administer TT treatments.

Limitations include the use of visual analogue scales as the only measure of pain and

distress and possibly random assignment of participants to practitioners. Random

assignment of practitioners to control for practitioner effects is reasonable theoretically,

but it differs from the usual practice of TT. The scientific benefits of randomization may

not outweigh the benefits of assessing TT in the context in which it is generally given and received in practice, i.e., by a given practitioner over time.

TT and wound healing. Wirth has conducted a series of studies on the effects of TT on the rate of wound healing. Following is a study representative of his work. In 1992, he investigated the effects of TT on the rate of healing of skin punch biopsy wounds in 44 healthy college students randomized into treatment and no treatment groups. A physician measured wound size on days 0, 8, and 16 using a standard direct tracing method and digitization system. Wounds were dressed and treated identically in both groups. The participants were exposed to daily 5-minute TT or mimic control sessions. The group treated with TT experienced significant acceleration of wound healing at days 8 and 16, as evidenced by decreased wound surface areas as compared to those in the control group. Adequate sample size, randomization to groups, and independent physician wound measurement are all methodological strengths in this as well as similar studies done by Wirth that have yielded similar results. The use of mimic TT in the control group would not appear to be a concern with the more objective and non-reactive outcome of wound healing.

TT and anxiety. In multiple studies, TT has been shown to decrease anxiety (e.g., Heidt, 1981; Quinn, 1984, 1989; Simington & Laing, 1993; Gagne & Toye, 1994; Olson & Sneed, 1995). Heidt (1981) measured the effects of therapeutic touch on anxiety in 90 patients hospitalized in a cardiovascular unit of a large urban medical center. An experimental pretest-posttest design was used with participants randomized into three groups consisting of 5-minute sessions of TT, casual touch, or no touch. The Speilberger Self-Evaluation Questionnaire, a well-established measure of state anxiety was used,

although the reliability and validity of this instrument were not reported for Heidt's study. Individuals who received TT experienced a statistically significant reduction in state anxiety. Participants did not experience a significant reduction in anxiety following the casual touch or no touch sessions. This was a well-designed and executed study. Sufficient sample size, treatment randomization, a reliable and valid instrument, and appropriate statistical analysis provided methodological rigor. The researcher did administer the TT treatments while a research assistant collected data. However, the research assistant was also responsible for randomization so she was not blinded to group assignments thereby introducing potential bias.

In a related trial, Quinn (1984) found that individuals treated with a form of non-contact TT experienced a greater decrease in state anxiety than did individuals treated with a mimic control intervention. This was the first TT study to employ the mimic TT intervention designed by Quinn. Quinn was testing the "theorem that the effects of therapeutic touch do not depend on actual physical contact" (p. 42). This hypothesis was based on Martha Rogers' nursing theory, the Science of Unitary Human Beings. According to Rogers (1990), people are energy fields; thus the human energy field is contiguous with the environmental energy field and physical contact is not necessary for energy exchanges. Citing Rogers' conceptual system and Heidt's (1984) outcome of anxiety reduction in cardiovascular patients following TT, Quinn conducted an intervention that "was identical to Heidt's intervention except that in Heidt's study, the hands were placed *on* the subject's body" (p. 45). Quinn studied 60 males and females with cardiovascular disease in an urban medical center. Participants were randomized into the non-contact TT intervention group or the mimic intervention control group, which

consisted of the practitioner performing the same hand movements as TT practitioners but without attempts to center, assist the participants, attune to the condition of the participant, or direct energy. Following a 5-minute session, the individuals who received non-contact TT experienced a greater decrease in posttest state anxiety than did those in the control group. Quinn concluded that because physical contact was not necessary for TT to reduce anxiety, study findings provided support for Rogers' energetic conceptual system. Another potential conclusion is that many individuals are uncomfortable with physical touch, thus, a non-contact intervention would be less anxiety provoking. This study was based on a sound theoretical framework and included an adequate number of participants, a reliable and valid measure of state anxiety, and attention to conducting TT and mimic TT sessions identically. Additionally, the researcher collected data while a total of four nurses administered the TT and mimic TT sessions. The nurses who administered the mimic sessions had no prior knowledge or training in TT.

In 1989, Quinn conducted a second investigation testing the theory of TT as energy exchange. Quinn hypothesized that if TT was based on energy exchange, eye and facial contact should not be necessary for manifested effects. This hypothesis was not supported. A total of 153 patients scheduled for next-day open-heart surgery were randomized to one of three groups: TT, a mimic control intervention (MTT), or no treatment, each lasting 5-minutes. The MTT was the same procedure used by Quinn in the aforementioned study. This intervention was judged to be indistinguishable from TT when observed directly by seven naïve observers and 40 naïve observers watching a videotape. During the 5-minute sessions, practitioners were asked to avoid eye and facial contact with participants. Measures included state anxiety, blood pressure, and pulse. There were

no statistically significant physiological changes among the groups. Decreases in posttest state anxiety scores were greatest in the TT group but also did not reach statistical significance. Quinn concluded that eye and facial contact may be a necessary catalyst for energy exchange in TT. The strengths of Quinn's 1984 investigation are also found in this follow-up study. The question of the mechanism of action of energy therapies such as TT remains unanswered.

In a double-blind, three-group experimental trial, Simington and Laing (1993) found that individuals treated with TT in the form of a back rub experienced significantly less state anxiety when compared to individuals who received a back rub without TT. They studied 105 institutionalized elders. Because of pilot data and other evidence suggesting that pretest measures can bias posttest measures, the researcher chose only posttest measures for this study. Participants were randomly assigned to one of three groups: receiving TT in the form of a back rub, a back rub without the focusing and intent of TT, or a back rub done by a nurse with no knowledge of TT. Participants were unaware of group assignment and were all treated as similarly as possible. The research team consisted of three individuals. One research assistant, blinded to the interventions, assisted participants in completing the state anxiety instrument. The other assistant, a registered nurse with no prior knowledge or training in TT, randomly assigned participants to groups and performed the back rub in one of the control groups. The investigator, a registered nurse and TT practitioner, administered the TT treatments as well as the second control group consisting of a back rub with no intention to center or direct the flow of energy. No significant baseline differences were found among the groups on key variables. The mean state anxiety score for the participants who received a back rub with TT was

significantly lower than the mean scores in the other two groups. This investigation

included a clearly stated theoretical framework, adequate sample size, treatment

randomization, blinding, limited practitioner/participant bias, and a reliable and valid

anxiety instrument. However, equivalence among groups cannot be evaluated without

pretest measures.

Gagne and Toye (1994) studied the effects of TT and relaxation therapy (RT) on

anxiety reduction. A group of 31 hospitalized psychiatric patients were randomly assigned

to one of two treatment conditions, TT or RT, or to the mimic TT placebo condition

designed by Quinn (1984). Participants were treated with two sessions in a 24-hour

period. TT and mimic control sessions lasted 15 minutes and were administered by a nurse

or nursing assistant. The RT intervention lasted 25 to 30 minutes and was administered by

a chaplain, according to a commonly used technique developed by Benson. Measures

included experienced anxiety (measured by the State-Trait Anxiety Inventory), a 30-

second frequency count of extraneous physical movement counted by research-trained

nursing staff, and a 10-item questionnaire entitled, "Final Summary," assessing the

participant's confidence in the treatment and the practitioner. Average pre-treatment

expectation of a positive outcome did not differ among the three groups. Using

multivariate analysis of variance, a significant reduction in experienced anxiety was found

in both the TT and RT groups, but not in the control group. The authors concluded that

larger scientific trials are needed before TT should be used in routine in-patient psychiatric

care, but the study provides evidence of the potential of both TT and RT to

decrease anxiety in this population. This study was well designed including adequate

sample size, treatment randomization, attention to practitioner-participant interaction effects, and consideration of covariates.

Olson and Sneed (1995) conducted a four-group, repeated measures experimental trial investigating the effects of TT on anxiety in 40 healthy professional caregivers who were enrolled in university-based nursing or health-related graduate programs. The participants were divided into high- and low-anxiety groups and further into TT or no treatment control groups. The effectiveness of TT in reducing anxiety as well as the assessment of concurrent validity of three measures of anxiety were the foci of this study. Anxiety was measured using two well-established anxiety measures as well as a visual analogue scale. The three psychometric measures (Profile of Mood States, Spielberger's State/Trait Anxiety Inventory, and a visual analogue scale) were highly correlated, but there were no statistically significant findings related to the effect of TT. No significant differences were found between the treatment and control groups; however, subgroup sizes were too small increasing the possibility of a Type I error.

TT and stress response. The effect of TT on stress reactivity has been examined in at least two trials. In a double-blind clinical trial, Randolph (1984) assessed the physiological response to stressful stimuli following TT in 60 healthy female college students. The physiological response was measured by skin conductance level, electromyography for muscle tone, and skin temperature. Participants were randomly assigned to receive non-contact TT or physical touch. Baseline measures were obtained on all participants, then they all watched a 13-minute stressful film while the experimental group received TT and the control group received physical touch in the form of a nurse's hands on the participant's lower back and abdomen. Those nurses performing TT centered

and attuned to the participants with the intention of therapeutically assisting the participant, while those nurses performing physical touch simply touched the participants on the lower back and abdomen. The nurses administering physical touch were not trained in TT techniques. Physiological response was measured again 8 minutes into the film at its most stressful point. Following the determination of baseline equivalence between the two groups, the hypotheses of the study were tested with analysis of covariance using baseline levels as covariates. None of the hypotheses were supported. The two groups were physiologically similar at baseline and both experienced significant stress in response to the film that was not attenuated by either of the interventions. Once again, this was a well-designed investigation that did not demonstrate a significant effect of TT (or physical touch) on anxiety levels.

Kramer (1990) examined the effect of TT on the stress response in children. A sample of 30 hospitalized children aged 2 weeks to 2 years were "selected" over a 5-month period and treated with either TT or casual touch. Randomization was not mentioned in the published report. Physiological response was assessed using a tool developed by the researcher for this investigation entitled "Physiological Measure of Relaxation in Response to Touch (PMRRT)," comprised of pulse, peripheral skin temperature, and galvanic skin response measurements. The intervention was done when the parent was not present, usually between the hours of 6 a.m. and 2 p.m. During a stressful procedure, children were treated with either TT, including centering and intending to influence the energy field, or casual touch consisting of stroking or patting the child's head, torso, or upper arms for 6 minutes. The PMRTT was administered 3 minutes and 6 minutes into the two interventions. The authors concluded TT significantly reduced

children's distress following stressful experiences, as evidenced by more rapid and greater decreases in scores on the PMRTT in the children who received TT as compared to those who received casual touch. Findings of this study must be interpreted with caution because this was not a well-controlled trial. Sample size and treatment randomization were not mentioned in the published report. Reliability and validity of the PMRTT were not mentioned. Also, the researcher administered the treatments and collected the data, possibly introducing bias.

TT and the grief response. At least two studies have investigated the effects of TT on the grief response. Quinn and Strelkaskaus (1993) investigated the effect of TT on bereavement. This particular study also investigated the effect of TT on immune function and will be discussed in detail in a subsequent section. In a doctoral dissertation, Robinson (1995) investigated the effects of TT on the grief experience in a convenience sample of 22 recently bereaved adults. This investigation was based on the premise that grief adversely affects physical and mental well-being and perhaps TT could attenuate these effects. Participants were randomly assigned to receive either TT or sham (mimic) TT. Each group consisted of 11 individuals who received three consecutive sessions. The time frame for the TT sessions was not reported. Additionally, it was not clear whether the researcher administered the TT and sham TT sessions. The Grief Experience Inventory (GEI) was used to assess the grief experience, but information on the reliability and validity of this instrument were not included in the abstract. Data were collected prior to the first session and following the third session, as well as at 1-week and 9-weeks following the interventions. Participants were also asked to describe their perceptions of the effects of TT on the grief experience at 9-weeks. Descriptive statistics, repeated

measures analysis of variance, and a summary of subjective responses were used to analyze the data. The participants who received TT experienced more favorable effects compared to controls on their grief processes, as evidenced by improved scores on the GEI as well as verbal reports of improvement in their grief responses. The author concluded that TT had a beneficial effect on the grief experience, but investigator bias cannot be ruled out in this study.

Qualitative explorations into TT. Three qualitative inquiries exploring the subjective experience of TT have been published in the literature. The knowledge gained in these explorations provides insight into the effects of TT as experienced by both the practitioners and recipients. Additionally, qualitative explorations, while not providing generalizable results, do provide information for theoretical consideration when interpreting data in similar populations as well as directions for future research. Heidt (1990) used the constant comparative method to generate a grounded theory explaining the experience of TT for seven nurse-recipient dyads. The researcher observed and made extensive notes during one TT session, then interviewed each nurse and recipient about their experiences. The findings were characterized by consistent descriptions of interviewees opening themselves up to the flow of universal life energy. There were three major categories of experiences: (a) opening intent, or allowing oneself to focus on reestablishing the movement of universal life energy; (b) opening sensitivity, involving assessing the quality of energy flow; and (c) opening communication, or participating in a healing relationship that "unblocks, engages, and enlivens" one's energy flow (p. 180).

Samarel (1992) conducted a phenomenological investigation into the experience of receiving TT. Data were generated through one unstructured interview followed by a

second clarifying interview of 20 individuals who had received TT. The participants'

descriptions fell into three time-related categories: experiences before TT treatment,

experiences during TT treatment, and experiences after TT treatment. Each category

contained specific elements. Prior to TT, participants described physiological needs,

mental/emotional needs, and spiritual needs. During TT treatment, participants described

self-awareness and other-awareness consisting of altered perceptions related to themselves

as well as others. Following TT, participants described personal changes that lead to

fulfillment in the physiological, mental/emotional, and spiritual realms. According to the

author, "the lived experience of TT was described as a linear process initiated by the

participant's decision to seek treatment" (p.651). The process continued through one or

more treatments and continued to make a difference in the participant's lives. TT was

experienced as a multi-dimensional process that fostered personal growth and well-being

over time.

Sneed and colleagues (1997) interviewed 11 female graduate students after the

second of two TT sessions. During data analysis, five categories emerged that described

the lived experience of the recipients who had no prior experience receiving TT. The five

categories were relaxation, physical sensations, cognitive activity, emotions, and

spiritual/transcendent experiences. All participants reported being relaxed and

experiencing physical sensations and cognitive activity during the TT sessions. Physical

sensations included "warmth", "goose bumps," and "tingling," among others. Cognitively,

participants thought about the process of TT and what was occurring while their eyes

were closed. A few participants expressed emotional or spiritual experiences. Participants

generally reported feeling "good" or "wonderful," but one participant reported feeling

uncomfortable being the focus of such intense attention. Four participants described spiritual or transcendent experiences such as feeling more centered. The authors theorized that perhaps "the sensations associated with TT may occur developmentally," with deeper experiences occurring when a recipient becomes more familiar with TT (p. 243).

The qualitative explorations done by Heidt (1990) and Samarel (1992) were appropriately designed qualitative studies with attention to rigor and trustworthiness of the data and findings. These explorations provide insight into the experience of giving and receiving TT. The third exploration involved interviews by the TT practitioner, followed by content analysis. The third study lacked adequate rigor and must be viewed with caution.

TT and well-being. In a time-series design, Giasson and Bouchard (1998) examined the effect of TT on well-being in 20 individuals with terminal cancer hospitalized in a university-affiliated hospital for palliative care. Participants were assigned randomly to either a TT intervention group or a control group. The 10 participants in the treatment group received TT on three consecutive days while the control group experienced periods of rest for the same duration as the TT session (15-minutes) at the same time of day. During periods of rest, the researcher was present but focused on mathematical equations to avoid intentional attention to the participant. Sessions were consistently conducted 1 hour following analgesic medication. Participants completed the Well-Being Scale on day 1 for a baseline measure and before and after sessions on days 2, 3, and 4. The Well-Being Scale is a visual analogue scale evaluating several indicators of physical and emotional comfort. Each of nine indicators (pain, nausea, depression, anxiety, shortness of breath, activity, appetite, relaxation, and inner peace) is set up on a 10-cm line with anchor words

to describe the end points of the scale, for example, "no pain" (0) to "severe pain" (10).

This scale demonstrated adequate internal consistency. Using chi-square and t-tests, no

significant differences were found among the groups on any demographic or medical

variables. No significant baseline differences were found for sense of well-being and mean

dose of analgesics or anxiolytics. Using repeated measures analysis of variance, individuals

in the TT group experienced statistically significant increases in well-being compared to

those in the rest period control group. Attention to methodological rigor included random

group assignment, homogeneity evaluations of the two groups, consideration of analgesic

and anxiolytic medications as covariates, control of environmental conditions during the

sessions (noise, interruptions, and temperature), and adequate TT practitioner training and

experience. The major limitations were small sample size and the potential of unconscious

influence of the researcher/practitioner who both administered treatments and collected

data.

TT and immune function. The effects of TT on immune function have been

investigated in three studies. One doctoral candidate explored the effects of TT on coping

response and immune function in 20 HIV-seropositive males (Garrard, 1995). Participants

were matched according to age, pharmacological therapy, and CD4+ lymphocyte counts,

then randomly assigned to either the experimental or sham (mimic) TT group. Coping

responses were measured using the Coping Resource Inventory (CRIS), which yields a

global score called the Coping Resource Effectiveness Score. The CRIS is comprised of

15 subscales. Internal consistency of the CRIS was assessed and found to be sufficient on

each of the subcales, with coefficient alpha scores ranging from .84 to .97. Test-retest

reliability yielded a high level of stability (r=.95). TT as well as sham TT was administered

by a single practitioner certified in TT. All sessions lasted 20 minutes; TT sessions consisted of a 5-minute assessment followed by 15 minutes of treatment in which the practitioner redirected the flow of energy. The sham treatment consisted of the practitioner entering the participant's room, standing at the head of the bed, then leaving the room 20 minutes later without having done any TT. Participants were blinded to group assignment. They wore sleep masks and headphones during sessions. CD4+ lymphocyte counts and coping effectiveness were assessed at baseline and at 3, 6, and 9 weeks. The specific number of sessions was not specified. However, the author stated that 9-week measures were done 3 weeks following the cessation of sessions. Using analysis of variance, statistically significant increases were found at week 9 in CD4+ cell counts and overall coping effectiveness in the participants who received TT. Findings were not statistically significant at weeks 3 or 6. Even with a small sample size, this study demonstrates strength in the areas of matching participants for potential covariates, treatment randomization, blinding, and the use of a reliable and valid coping instrument. However, post-intervention CD4+ cell counts were displayed in a graph so that actual values are not easily determined. In viewing the graph, elevations in CD4+ cell counts appear to be modest and are not increased consistently in all participants, making it difficult to determine any potential clinical significance of this finding.

Two trials investigating the effects of TT using a PNI framework have been published in peer-reviewed journals. Olson and colleagues (1997) discovered a statistically significant trend toward enhanced immune function following TT in healthy college students experiencing the stress of upcoming graduate entrance exams. A sample of 20 healthy medical and nursing students were randomized to the TT treatment group or the

no treatment control group. An experienced TT practitioner who was not responsible for data collection did TT. Measures included three psychosocial instruments (Spielberger State/Trait Anxiety Inventory [SSTAI], the Impact of Events Scale [IES], and the Profile of Mood States [POMS]), a demographic and health habits questionnaire, and quantification of antibody response to the Haemophilus influenzae vaccine, serum immunoglobulin levels (IgG [including subclasses], IgA, IgM), and lymphocyte subsets. Using t-tests, differences between groups were significant for a decrease in serum IgA and an increase in serum IgM, but no significant differences were noted in serum IgG or its subclasses. Changes in lymphocyte subset assays were not significant, including CD25+ levels, which were measured as a correlate of interleukin-2 receptor expression. There were no differences between groups in levels of antibodies to Haemophilus influenzae. Further, statistically significant differences were not detected on any of the psychosocial measures. The authors cited the small sample size and the presence of confounders such as dietary changes during exams as possible explanations for the predominantly non-significant findings. Additionally, the possibility that TT does not affect immune function must be considered.

Quinn and Strelkauskas (1993) conducted the most comprehensive trial published to date on the effects of energy work using a PNI framework. They investigated the effects of TT on certain psychological and immunological parameters in bereaved individuals. The investigators measured the effects of TT on practitioners as well as participants to explore the premise that energy-based techniques affect both the practitioner and the recipient. Despite some intriguing findings in Quinn and Strelkauskas's investigation, it was not designed rigorously and included only four

participants and two practitioners. Outcome measures included state anxiety, affect, effectiveness of TT treatment, time perception, and four measures of immune function, namely, lymphocyte subset composition; responsiveness toward foreign cells as shown by mixed lymphocyte reactivity and cell-mediated cytotoxicity; lymphocyte stimulation using phytohemagglutinin (PHA), concanavalin A, and pokeweed mitogen; and natural killer cell assays. Participants experienced a 29% average decrease in state anxiety as measured by the SSTAI. There was not a meaningful change in the anxiety scores of the practitioners, perhaps because their anxiety scores were very low throughout the study. In participants and practitioners, there were significant increases in all positive dimensions of the Affect Balance Scale as well as significant decreases in all negative dimensions.

Using the Effectiveness of Therapeutic Touch Scale, the participants treated by one practitioner scored 54% higher than did those treated by the second practitioner. However, the practitioners differed in their levels of TT experience and amount of TT practice time per week, and the more experienced practitioner received the higher scores. Practitioners and participants were asked to estimate the amount of time that elapsed during their session as a measure of the altered consciousness that is theorized to occur with TT and HT. The participants treated by the more experienced practitioner perceived greater lapses of time, implying greater alterations in consciousness, according to the investigators. All participants and one practitioner experienced a decrease in the percentage of suppressor T-lymphocytes (CD8+). The more experienced practitioner had a low suppressor T-cell percentage at baseline and this finding persisted throughout the study. Further evidence of enhanced immune function among participants included improved lymphocyte responsiveness to foreign cells as well as heightened lymphocyte

proliferation in response to mitogens and increased natural killer cell activity. Missing data made it difficult to assess these immune measures in the practitioners. Because of missing data and the small sample size, it is not possible to fully interpret the data in this study. However, it provides a beginning for the exploration of the effects of energy work in the context of the PNI paradigm.

This study exploring the effects of HT will build on and expand the strengths of Quinn and Strelkauskas's (1993) investigation while avoiding the weaknesses of their work. First, the experimental design proposed here allows for extensive scientific control. Second, an adequate number of participants will be included. Third, HT practitioners will all be nurses who have completed at least Level 3A of HT training, signifying adequate HT training, and will have comparable experience levels.

Summary of HT and TT research. In a review of the state of the research on the effects of TT spanning 23 articles in 14 refereed journals, Easter (1997) concluded, "the findings of the research indicate positive regard for the use of Therapeutic Touch. All research points to the need for further study in this area. Research methods used to date are satisfactory, but it would behoove researchers to be more rigorous in research methodologies to produce a truly scientific contribution to the body of nursing literature" (p. 163). The research reviewed here provides a representative view of the current state of the science of HT and TT research. Consistent with Easter's review, the majority of the research yields positive outcomes for these therapies. However, frequently the researcher's conclusions are not congruent with the data presented. Additionally, Easter's call for increased scientific rigor, especially in quantitative investigations, is corroborated in this literature review. If research exploring the effects and experiences of HT and TT is

to meaningfully contribute to the body of nursing literature, attention to appropriate research design and methods are necessary. The major limitations in the research reviewed include inadequate sample sizes, lack of treatment randomization and control groups (especially in the studies published in the HT International Research Survey), possible practitioner-participant effects when the practitioner is also the researcher, mimic TT sessions used as the control condition, potentially unreliable and invalid instruments, underdeveloped theoretical frameworks, liberal interpretation of data, and failure to consider the presented theory may be wrong when confronted with inconsistent data. The clinical trial proposed herein involves consistency between the research questions and methods as well as a sound theoretical framework and adequate scientific rigor. Thus, this study should provide valuable information on the effects of HT in individuals with HIV disease.

Well-being

Current conceptions of well-being are based in part on Larson's (1978) meta-analytic review of trials spanning 30 years using a multiplicity of measures of affect. In Americans over age 60, negative life situations such as poor health were correlated negatively with well-being. Brook and colleagues (1979) also found negative correlations among subjective well-being, age, and general health ratings. Monk (1981) found that "labeling" individuals with the diagnosis of hypertension decreased psychological well-being and asserted this may be a phenomenon in any chronic illness.

While there is accumulating evidence that negative affect is associated with immunosuppression (Kemeny & Dean, 1995), there is relatively little research concerning positive affect. It may be possible to impact positively physiological variables with positive

affective changes in individuals with HIV disease, given that some studies have shown positive affective states to be associated with improved immune function and the opposite for negative affective states. In one set of studies, T-lymphocyte proliferative response to the mitogen PHA was enhanced by positive mood states and diminished by negative mood state (Futterman, Kemeny, Shapin, & Fahey, 1994; Kemeny et al., 1994). In an exploratory study of the effects of stress and psychological status on humoral immune response, Snyder and colleagues (1990) found that psychological well-being was positively correlated with postimmunization IgG levels and the opposite for psychological distress. A total of 89 healthy female college students were immunized with keyhole limpet hemocyanin (KLH). Life stress, psychological status, and serum IgG levels were measured immediately prior to immunization and 3 and 8 weeks following immunization. Sample size was calculated to be large enough to demonstrate a medium effect size. Participants with greater psychological well-being had significantly higher IgG levels at all three measurement times compared to those with lower psychological well-being.

Several issues arise when evaluating the outcomes of trials investigating positive affective states such as enhanced well-being. First, empirical evidence to date remains inconclusive and contradictory. For example, Futterman and colleagues (1994) found that positive as well as negative affective states enhanced NKC cytotoxicity. Second, none of these studies has investigated well-being as this trial seeks to do. Correlates of well-being such as coping effectiveness and hardiness have been investigated, but no global indicator of general well-being has been included. Third, many studies have been fraught with inadequate sample sizes and methodological flaws (McCain & Zeller, 1996) that this trial avoided. Finally, none of these trials have evaluated the effects of complementary

therapies on the PNI parameters measured in this trial. In this study, relationships among well-being, neuroendocrine mediation, and immune function were further investigated in individuals with HIV disease.

Neuroendocrine Measures

Serotonin (5-HT). 5-HT is a neurotransmitter and hormone produced in the central nervous system (CNS) that influences mood and well-being (Miller & Keane, 1987). Neurotransmitters are signal molecules that mediate communication between the endocrine, nervous, and immune systems. Research indicates that serotonergic abnormalities are involved in the pathogenesis of anxiety and dysphoric states. Individuals experiencing anxiety and/or dysphoria exhibit alterations in serotonergic functioning, specifically, exaggerated re-uptake of 5-HT by CNS neurons. Selective serotonin re-uptake inhibitors (SSRIs) such as fluoxetine (Prozac) have been useful in treating anxiety and dysphoria because they interfere with the re-uptake of 5-HT in the CNS. Research into the dysphoric states associated with premenstrual syndrome (PMS) indicated improvement in this negative affective state with similar medications due to the release of central 5-HT and the prevention of its re-uptake (Brzezinski et al., 1990). Generally, increasing the amount of centrally circulating 5-HT lessens anxiety and elevates mood (Baldwin & Rudge, 1995).

Serotonin is also gaining acceptance as an immune modulator. Smith and colleagues (1991) reviewed the role of 5-HT in immune responses. In peripheral blood, 5-HT is localized in platelets and released at sites of injury. Lymphocytes possess a high affinity binding site for 5-HT. Mast cells can also take up and release 5-HT. With injury or inflammation, mast cells release 5-HT which helps mediate local immune processes.

Further, 5-HT augments NK cell cytotoxicity directly as well as indirectly through monocyte stimulation and by diminishing the suppressive activities of macrophages. Basically, 5-HT is required for optimal T-lymphocyte activation as well as macrophage accessory function for T-cell activation (Sosroseno, 1995; Young & Matthews, 1995). To date, research on serotonin has focused on negative affective states such as depression and PMS. No research has been found investigating serotonin and positive affective states.

DHEA and cortisol. It is thought that severe illness causes an adaptive adrenocortical shift manifested by increased cortisol and decreased DHEA concentrations resulting in an increase in the cortisol/DHEA ratio (Parker, Levin, & Lifrak, 1985). In HIV disease, cortisol remains elevated at all levels of infection. There is a negative linear correlation between CD4+ lymphocyte counts and cortisol whereas there is a positive linear correlation with DHEA. Additionally glucocorticoids, including cortisol, are associated with alterations in cytokine production and the progression of HIV disease perhaps because of a shift from a type 1 to a type 2 cytokine pattern as well as programmed cell death (Clerici et al., 1997).

Recently it has been suggested that psychological stress, by virtue of increased cortisol and decreased DHEA, may be associated with HIV disease progression (Clerici & Schearer, 1994; Jacobsen, Fusaro, Galmarini, & Lang, 1991; Mulder et al., 1992). Whereas cortisol stimulates HIV replication and augments humoral immune function, DHEA has a reciprocal effect that includes inhibition of HIV replication and augmentation of cellular immune function (Regelson , Loria, & Kalimi, 1994). Reducing cortisol levels may contribute to the attenuation or reversal of disease progression.

While there have been no reports concerning positive affect and cortisol/DHEA it is postulated that enhanced well-being may influence this ratio and thereby enhance cellular immune function. If negative affect increases cortisol and decreases DHEA, thereby impairing immune function, then perhaps positive affect decreases cortisol and increases DHEA, thereby enhancing immune function.

Immune Measures

Lymphocyte subsets. T-lymphocytes may mediate important host responses to HIV infection including cytotoxicity and suppression of HIV as well as pathogens responsible for opportunistic infections (Carr, Emery, Kelleher, Law, & Cooper, 1996). Cellular subsets designated CD4+, CD8+, CD57+, and the mixed subset CD8+/CD57+ are useful enumerative measures because of their roles in immune dysfunction in HIV disease. These four were chosen because the level of CD4+ lymphocyte levels is a well established marker of HIV disease status and progression, and CD8+, CD57+ and the mixed subset of CD8+/CD57+ lymphocytes contribute information about numbers of cytotoxic immune cells. CD8+ lymphocytes are a subset associated with cytotoxic and suppressor functions. CD57+ lymphocytes are cytotoxic cell markers, thus the mixed subset of CD8+/CD57+ contains both suppressor and cytotoxic cells. The CD4+ and CD8+ lymphocytes are the most frequently studied of the subsets. For example, it is well documented that CD8+ cells possess suppressor as well as cytotoxic functions and are the principle specific mediator of non-HIV virus eradication. Non-cytotoxic CD8+ T-cells may play a vital role in preventing HIV disease progression. According to Levy and colleagues (1996), the CD8+ antiviral response occurs soon after infection and is maintained in asymptomatic individuals. Finally, alterations in cytokine production are

associated with CD4+ and CD8+ lymphocyte subsets (Rodriguez, Yano, Eylar, & Yamamura, 1997).

Lymphocyte proliferation. Clerici and Shearer (1993, 1994) have extensively studied the progressive dysfunction of the immune system in HIV disease. Viral pathogenesis involves a progressive loss of T-helper cell function involving both CD4+ and CD8+ lymphocytes. The T-lymphocyte response to recall antigens such as tetanus toxoid is the first function lost, followed by loss of T-helper cell response to allogeneic-major histocompatability complex, and finally, loss of T-helper cell reactivity to phytohemagglutinin(PHA). Lucey and colleagues (1991) studied over 600 HIV-infected but asymptomatic individuals and found that peripheral blood mononuclear cells (PBMCs) from 34% of the individuals responded to all three stimuli, 40% were selectively unresponsive to recall antigens, 11% responded to PHA only, and 15% were unresponsive to any of the stimuli. Progressive defects in the response to these stimuli are positively correlated with disease progression and a more rapid decline in CD4+ T-cell counts. Improvement of T-helper cell function independent of CD4+ counts has been observed in individuals on HIV pharmacotherapeutic protocols (Clerici etal., 1992). These positive changes in T-helper cell function correlated with a lower incidence of opportunistic infections, once again independent of CD4+ counts.

NK cell cytotoxicity. NK cells are large granular lymphocytes and are spontaneously cytotoxic to tumor and virally infected cells. Abnormalities in NK cell function in HIV disease include changes in cytotoxic function, cell subset distribution, cytopathology, and cytokine regulation (Brenner et al., 1989). Because HIV disease first manifests in qualitative immune dysfunction (Clerici et al., 1989), functional, rather than

enumerative immune measures may be more accurate indicators of disease status over the disease trajectory (Nott et al., 1995). Additionally, functional indicators of immune status, particularly NK cell cytotoxicity, may be more sensitive to psychosocial factors than are enumerative immune measures (Kiecolt-Glaser & Glaser, 1992; Schulz & Schulz, 1992). However, it must be acknowledged that functional assays are performed in vitro in an environment that is markedly different from in vivo measures in terms of endocrine and other physiological influences, making it difficult to know how well these assays reflect in vivo cellular functioning.

Cytokines. According to Clerici and Shearer (1993, 1994), an immune system imbalance occurs in HIV-infected individuals that generally weakens the immune system and accelerates the progression to AIDS. They proposed that a shift from "type 1" to "type 2" cytokine regulation was a critical step in the progression of HIV infection. Type 1 regulation primarily involves the cellular immune system and type 2 the humoral immune system. A type 1 pattern enhances cytotoxic function to protect the body against infection by viruses and intracellular pathogens, whereas a type 2 pattern enhances antibody and allergic responses. Ideally, optimal function of both types of responses is desired to control HIV replication and disease progression. However, in some cases, cross-regulation of these two responses fosters stimulation of one at the expense of inhibition of the other. Thus, as the type 1 response is progressively diminished in HIV disease, the type 2 response is enhanced and the body loses its ability to fight opportunistic infections (Mosmann, 1994). Manipulation of the cytokine network is currently thought to be a potentially important strategy in the control of HIV replication and thus disease progression (Poli & Fauci, 1996).

In this study, a type 1 cytokine pattern will be represented by IL-2 and TNF-α and a type 2 cytokine pattern will be represented by IL-4 and IL-6. Although research does not consistently support a type 1 to type 2 shift, Shearer and Clerici (1993, 1994) have presented some compelling findings. For example, IL-2 and other type 1 cytokines (IL-12, IFN-γ) have been shown to reduce apoptotic T-cell death as did antibodies against the type 2 cytokines IL-4 and IL-10. In contrast, IL-4 and IL-10 as well as antibodies against the type 1 cytokine IL-12 did not prevent, and in some cases increased, cell death. Also, antigenic stimulation in a dominant type 2 environment resulted in an increase in the proportion of dying cells, whereas these cells can be rescued if antigenic stimulation occurs in a dominant type 1 environment. Finally, Clerici and Shearer (1993) as well as Chehimi (1994) found that adding IL-12 to cultures of PMBC's from HIV-infected individuals restored cellular immune function, including NK cell activity, IFN-gamma production, and lymphocyte proliferation to recall antigens.

Currently, the cause of the shift from type 1 to type 2 regulation as well as other HIV-associated immune dysfunction is not known. While it is known that medication can help reverse immune dysfunction in some individuals, it is not known if other therapies will be useful. It was theoretically sound to suggest that therapies such as HT may support or augment the immune system by enhancing well-being, thereby increasing serum serotonin and DHEA and decreasing cortisol, and subsequently, helping to maintain type 1 cytokine regulation, inducing a shift from type 2 to type 1, and/or enhancing cellular immune function by other mechanisms.

Summary

According to Ader (1992), a leading researcher and founder of the PNI field, "an assessment of the clinical relevance of behavioral influences on immune function requires strategies that follow from a conceptual model of integrated processes of adaptation and a multi-determined concept of health and disease" (p. 6). Because of its grounding in PNI, this study entailed that kind of research strategy. There are no reports of research investigating the specific treatment and outcomes outlined here. HT and the outcomes measured were grounded solidly in the PNI framework, and there was adequate related theoretical and empirical evidence to support the investigation of the effects of HT on well-being, serum 5-HT levels, DHEA and cortisol, and immune function.

Chapter 3

Research Design and Methods

The purpose of this study was to ascertain the effects of HT on selected PNI

parameters in HIV-infected participants. It was hypothesized that HT would increase

participant well-being, which would increase subsequently both serotonin and DHEA and

decrease cortisol, and ultimately enhance immune function. This purpose was addressed

using an experimental pretest-posttest design comparing the effects of HT on selected

psychoneuroimmunological parameters in individuals living with HIV disease. A wait-list

crossover control group was used to enable every participant to receive treatment.

Participants who agreed to participate voluntarily in the study were enrolled and

randomized to (a) the wait-list control group or (b) the immediate treatment group. Time

1 measures were done immediately before the first treatment session or beginning of the

waiting period, and time 2 measures were done immediately following the last treatment

session or the end of the waiting period (and simultaneous start of the first treatment).

Immediately before the initial treatment session and immediately following the final

(fourth) treatment session, participants completed the General Well-Being schedule

(GWB), the Faces Scale, the Human Field Image Metaphor Scale (HFIMS), the brief

Profile of Mood States (POMS), and the Impact of Events scale (IES), and had blood

drawn for 5-HT and immune measures. Additionally, immediately before and after each

session, and 4 to 6 hours after receiving HT, the Faces Scale was completed by

participants. Salivary samples for DHEA and cortisol were collected by participants upon arising the day of data collection. There were five certified HT practitioners, each performing 20-25 HT treatments, for a planned study total of 120 treatments (30 participants each receiving 4 treatments).

The target population was males living with HIV disease who met the enrollment criteria. Because of the small sample size and the effects of gender on neuroendocrine and immune measures, women were not included in this study. A sample of 30 individuals was recruited to receive the HT intervention. Simple random sampling was used to assign participants to the wait-list or immediate treatment groups. All participants had to have been male, at least 18 years of age, able to read and speak English, and deemed to be physically able to attend sessions (as demonstrated by Karnofsky performance scores of at least 60, [Appendix C, Attachment 3]). Participants could not have been taking steroids or immunomodulatory drugs (including cytokines, thymic derivatives, and antineoplastic agents, but excluding HIV-related antiretroviral drugs). Additionally, participants must have had a CD4+ lymphocyte count of at least 50 cells per microliter within 3 months of study participation in order to have immune measures drawn. Potential participants were screened and excluded for (a) significant psychiatric illness, including active psychoses, dissociative disorders, severe or unstable depressive disorders, and organic mental disorders or (b) cognitive impairment, evidenced by a score of less than 20 on the Cognitive Capacity Screening Examination (Jacobs, Bernhard, Delgado, & Strain, 1977 [Appendix C, Attachment 4]). It was acknowledged that antiviral medications are immunomodulatory. Therefore, participants were excluded if there had been antiretroviral medication regimen changes (dose and/or drug) within one month prior to study

enrollment. Additionally, controlling within subject variability was controlled by ensuring that all participants who had antiretroviral medication changes (including dosages) following enrollment were excluded from the immunological analyses. Beyond these criteria, potential participants were not excluded on the basis of their disease status.

Human subjects: Recruitment, protection, and retention. Following approval of the study by Committee on the Conduct of Human Research of Virginia Commonwealth University, recruitment flyers were distributed in the Medical College of Virginia Hospitals Infectious Disease and the Fan Free Clinics, as well as physicians' offices. Interested individuals were screened and enrolled by the investigator. Participants were informed fully about the study in accordance with all expectations for the protection of human subjects. Those participants who volunteered to participate in the study were identified only by an arbitrary identification (ID) number. A file containing the participant's name, informed consent document, and corresponding ID number will be kept in a locked cabinet in the investigator's office and will be accessible to the investigator and dissertation chair only. Immediately following enrollment, participants were randomly assigned to the wait-list control group or the immediate HT treatment group. To enhance retention, participants were paid $50 upon completion of the study. Wait-list participants were paid $25 at the end of the wait-list period and an additional $50 following their final HT session. Additionally, participants were contacted by phone each week to remind them of their appointments.

Demographic Variables and Potential Cofactors

During enrollment, pertinent demographic data were collected using a data record form (Appendix C). Additionally, enrollment procedures included data collection on two

critical cofactors: Centers for Disease Control (CDC) classification (CDC, 1992)

(Appendix C, Attachment 1) and the revised HIV Center Medical Staging Scale

(rHCMSS) score (McCain et al., 1998) (Appendix C, Attachment 2). The CDC

classification system has widely recognized clinical and research utility. It is a nominal-

level scale that rates categories of disease across three levels of clinical symptoms and

three levels of immunological status. Clinical symptoms are categorized as Stage A for

acute and asymptomatic infection, Stage B for non-life threatening and non-AIDS

opportunistic illnesses, or Stage C for AIDS-defining conditions including life-threatening

opportunistic illnesses. The three levels of immunological status are reflected by CD4+ T-

lymphocyte levels: 1= 500 or greater, 2= 200-499, and 3 < 200.

Despite its acceptance and frequent use as an indicator of HIV-disease

progression, the CDC scale provides limited information. For this reason, the rHCMSS

was also used as a measure of HIV-disease status and symptomatology (McCain et al.,

1998). The rHCMSS provides a measure of the progression of HIV-related

symptomatology that is not confounded by psychiatric symptoms or immunological status.

The original HCMSS was developed by Gorman and colleagues (1992) based on 1986 and

1987 CDC criteria which did not include HIV-related conditions specific to women.

Additionally, it was tested by physician providers only. The revised version is based on

1992 CDC criteria, includes updated Category B and AIDS-indicator conditions, as well

as delineated anchor definitions for progressive scoring within each of the four major

staging categories. According to McCain and colleagues, the validity of the rHCMSS was

assessed as part of a larger study in a sample of 124 individuals living with HIV disease.

Pearson's correlation between the rHCMSS and the CDC classification was .80,

demonstrating adequate construct validity. Validity was further supported by correlations

between rHCMSS scores and CD4+ count (r= -.44) and CD4+ percentage

(r= -.62).

Because the sample size was limited to 30 participants, potential covariates were

chosen carefully to reduce the confounding of excessive, redundant, or insignificant

cofactors. Although viral load is a potential covariate in HIV disease, viral loads were not

measured in this study because of financial limitations. Additionally, with current

pharmacological regimens for treating HIV infection, many individuals have undetectable

viral loads. Other potential cofactors include psychoactive drug use, excessive alcohol use,

age, amount and intensity of physical exercise, and malnutrition, as evidenced by weight

loss >10% of usual body weight. Baseline data were collected on all covariates to enhance

clarity and accuracy of the results. However, because of the limited sample size, it was

anticipated that the statistical model would allow inclusion of only the most critical

cofactors of rHCMSS score and CD4+ lymphocyte counts.

Independent Variable: HT

HT practitioners who participated in the study had completed at least level 3A of

HT training, signifying they had completed at least four of the five levels of HT training.

This criterion minimized variability among treatments by ensuring that practitioners had

similar training and extensive experience working with clients. Additionally, every attempt

was made to select practitioners with comparable amounts of experience and practice time

per week. HT practitioners were selected from the local pool of certified practitioners

based on their availability to provide treatments throughout the study. Participants' weekly

HT sessions lasted 20 to 30 minutes and included the chakra connection technique. HT

sessions began with the practitioner setting her intention to help the recipient. Chakra connection involves placing the hands on the participant's energy centers or chakras to assess, then balancing each of the seven major chakras (ground, sacral, solar plexus, heart, throat, brow, and crown). Chakra connection is a general technique that balances the overall energy field. The format of this technique is illustrated in Appendix B and was followed as precisely as possible to ensure equivalence of the HT treatments. HT sessions were conducted in a standard, private hospital room in the General Clinical Research Center (GCRC). Basically, the rooms consisted of a table, chair, and adjustable hospital bed.

To ensure understanding of and adherence to the HT protocol, the investigator met with the HT practitioners involved in this study prior to the onset of the study to review the protocol. The investigator then met with practitioners following the first HT sessions and prior to the beginning of subsequent groups of participants (wait-list participants' intervention) to review the protocol. HT practitioners were asked to follow the chakra connection technique as it appears in the standard HT manual. Additionally, they were asked to perform pre- and post-treatment assessments on each participant and record their observations on a standard HT assessment form (Appendix B, Attachment 1). These assessments were used to provide insight and clarification in data analysis and interpretation. At the first treatment session, participants were assigned arbitrarily to practitioners. Following this initial assignment, practitioners continued to work with the same participants to the extent possible.

Dependent Variables: Well-being, 5-HT, DHEA, Cortisol and Immune Measures

Psychosocial measures. Five psychosocial measures were used in this study including four measures of well-being as well as an illness-specific psychosocial instrument (included as Appendix D) to assess the immediate as well as cumulative effects of the intervention. The most direct measures of well-being were the General Well-Being schedule (GWB) and the Faces Scale. The GWB consists of 18 questions, whereas the Faces Scale is completed by circling a single face. The shorter format of the Faces Scale allowed assessment of well-being immediately before and after each treatment session while minimizing the workload of the participants. Additionally, single-item indicators may yield more valid data when the variable of interest is the participant's overall perception of an experience (Youngblut & Casper, 1993). No studies have been reported using either of these scales in the HIV population.

As a multi-item indicator the GWB is a comprehensive measure of well-being which reflects both positive and negative feelings on the six dimensions of anxiety, depression, general health, positive well-being, self-control, and vitality (McDowell & Newell, 1996). The first 14 items use 6-point response scales representing intensity or frequency and ask questions such as, "Have you been under or felt you were under any strain, stress, or pressure during the last month," with answers ranging from a score of "1" for the strongest agreement (e.g.,"Yes, almost more than I could bear or stand") to "6" for the strongest disagreement (e.g., "Not at all"). The final four items ask for responses using marks from 0 to 10 on a horizontal visual analogue scale to questions such as, "How concerned or worried about your health have you been during the past month?" Responses range from a low of "not concerned at all" to a high of "very concerned." Total scores

range from 14-124, with lower scores representing more distress and higher scores representing positive well-being. Responses also can be assessed according to the six individual subscale scores with a range of two to four questions comprising each subscale. Considering the complexity of issues relating to living with HIV disease, a scale that encompasses multiple aspects of well-being was not only appropriate, but also necessary in order to achieve a valid measure of well-being.

Monk (1981) assessed the 3-month test-retest reliability of the GWB in two different groups from data collected on adults aged 25-74 years who participated in the Health and Nutrition Examination Survey conducted from 1971-1974 and found reliabilities of .68 and .85. Fazio (1977) reported a 3-month test-retest reliability of .85 in a sample of 195 college students. Internal consistency of the GWB is consistently high, with Cronbach's alpha ranging from .88 to .95 (Fazio; Himmelfarb & Murrell, 1983). In the study conducted by Fazio, alpha coefficients were .91 for 79 males and .95 for 116 females. Himmelfarb and Murrell (1983) reported alpha coefficients of .92 in 109 older persons in inpatient psychiatric units and .88 for 279 elders living in the community. Fazio reported discriminant validity scores of .47 when the GWB was correlated with an interviewer's rating of depression, .66 with Zung's Self-rating Depression Scale, and .78 with the Personal Feelings Inventory—Depression.

The Faces Scale demonstrated an average test-retest reliability of .70 in Andrew and Crandall's 1976 test of the validity of over 30 measures of self-reported well-being in 222 adults. In this sample, the median validity coefficient for the Faces Scale was .82 when tested using a multimethod-multitrait investigation in which six aspects of well-being were assessed by four methods using structural modeling to partition variance. Andrews

and Crandall concluded that the validity score of the Faces Scale was among the top three of the instruments tested. In a review of research using single-item indicators, Youngblut and Casper (1993) found that these measures generally yielded acceptable reliability estimates and performed consistently well in validity testing. According to Hurny and associates (1996), "mood as a global concept can validly be assessed with a single-item scale" (p. 245). They asserted that single-item indicators are suitable for clinical trials when multi-item scales are less feasible, which is the case with measures before and after each treatment session. Although they emphasized that single-item scales capture only one aspect of a concept, this was not a major concern with this study because a multidimensional indicator was also being used.

The third measure of well-being was the 17-item short version of the Profile of Mood States (POMS) (Cella et al., 1987). The POMS is a widely used, standardized measure of mood comprised of 65 items which yield the Total Mood Disturbance Score (TMDS) as well as six subscale scores. The short version is preferred because of its ability to elicit a measure of TMDS, or positive/negative affect, efficiently and accurately. The original 11-item brief POMS was derived by factor analysis of the full POMS from a sample of 619 adults with various types of cancer, then replicated in a sample of 295 adults with lung cancer (Cella et al., 1987). In this population the brief POMS demonstrated a Cronbach's alpha of .91. Discriminant validity was supported in two groups of patients with specific cancers, pancreatic and gastric. Based on earlier data, the authors knew that scores in pancreatic cancer patients were significantly higher than those of gastric cancer patients, presumably because of a tumor-mediated paraneoplastic syndrome present in pancreatic cancer. When the data from these two subgroups were

analyzed, the mean scores were higher in the pancreatic cancer group compared to the gastric cancer group. Subsequently, six positive affect items (the original 11 items are all negative affect items) were incorporated into the brief POMS to produce the current 17-item scale.

The fourth measure related to well-being used in this study was the Human Field Image Metaphor Scale (HFIMS). The HFIMS was chosen for two reasons. First, it was developed based on the Science of Unitary Human Beings, a nursing theory applicable to HT because of its focus on humans as energy fields. Secondly, it is consistent with the conception of well-being as a reflection of perceived human potential (Dossey et al., 1995; Bradburn, 1969). The HFIMS is a 5-point Likert-type scale consisting of 25 metaphorical items beginning with "I feel." The potential range of scores on the HFIMS is 25 to 125. The higher the score, the clearer the field image. It has been postulated that clear field images are correlated positively with knowing participation in life choices and changes, especially those related to health and well-being. A blurred field image corresponds to a passive acceptance of life experiences.

The HFIMS is a reliable and valid measure of perceived potential and integrality. Psychometric properties of the HFIMS were assessed in a pilot study of 50 and a major study of 358 healthy adults. Final results yielded a 25-item scale with three factors that were labeled "expressions of clear human field," "expressions of a blurred human field image," and "integrality." In pilot testing the HFIMS demonstrated a Cronbach's alpha of .93 and in major testing, .91. Construct validity was assessed in both studies by correlating the HFIMS with the Index of Field Energy, a related but not identical instrument.

Using the Pearson product-moment correlation, a convergent validity score of .59 was found in pilot testing and .70 in major testing.

An additional psychosocial measure used in this investigation was the Impact of Events Scale (IES). The IES is a measure of illness-specific psychological distress. Mood is conceptualized in this study on a continuum anchored by positive and negative affect, or psychological well-being and distress. The IES was an appropriate measure in this clinical trial, in part because the other measures of well-being, while they also capture negative affect or distress, had not been previously tested in the HIV population. Using the IES, psychological distress related to living with HIV disease has been previously documented as avoidant and/or intrusive thought processes related to the illness (Ironson et al., 1990; McCain & Cella, 1995; McCain, Zeller, Cella, Urbanski, & Novak, 1996; Perry et al., 1992). The IES is a 15-item instrument comprised of two subscales, intrusion and avoidance, that yields an index of illness-related psychological distress. It was developed by Horowitz, Wilner, and Alvarez (1979) based on the premise that research on human responses to stress requires evaluation of serious life events as well as their subjective impact. The IES exhibits exceptional psychometric properties and is not confounded by physical symptoms (McCain & Cella, 1995; McCain et al., 1996). In a sample of 66 persons with stress response syndromes, the split-half reliability of the total scale was .86. Internal consistency of the two subscales was high, as evidenced by a Cronbach's alpha of .78 on the intrusion scale and .82 on the avoidance scale. A correlation of .42 between the intrusion and avoidance scale signified they are associated, but do not measure the same dimensions of distress. Test-retest reliability was assessed in a group of 25 physical therapy students before and after dissection of a cadaver. Test-retest reliability of the total

scale was $r=.87$, .89 for the intrusion subscale, and .79 for the avoidance subscale. The IES contains response options indicating the frequency of distressing (intrusive or avoidant) thoughts over the prior 7 days. Higher scores on the subscales of intrusive and avoidant thinking signify higher psychological distress.

Physiological measures. Pulse was measured by the HT practitioners before and after each session as a gross indicator of physical relaxation. Biological measures included salivary DHEA and cortisol, serum 5-HT levels as well as PBMC proliferative response to PHA, NK cell cytotoxicity, lymphocyte subsets (CD4+, CD8+, CD57+, and CD8+/CD57+), and selected type 1 (IL-2, TNF-α) and type 2 (IL-4, IL-6) cytokine levels. Serum 5-HT levels were drawn and processed by the staff of the GCRC. Immediately following the study, frozen samples were shipped to LabCorp for testing. Serotonin levels were assessed using high performance liquid chromatograpy (HPLC).

Salivary DHEA and cortisol were collected by participants upon arising the day of data collection and processed by the GCRC. Salivary DHEA has been validated as an indicator of the unbound fraction of plasma DHEA. Like salivary cortisol, unconjugated DHEA is liposoluble and rapidly diffuses from plasma to saliva, so that salivary concentration is not dependent on salivary flow rate. Mean salivary DHEA has been reported to be 392 pmol/L in healthy individuals (Lac, Lac, & Robert, 1993). Salivary cortisol is a reliable indicator of the biologically active, unbound fraction of circulating cortisol, with correlations between cortisol in saliva and blood typically greater than .90. Salivary cortisol concentrations accurately reflect changes in blood levels within two minutes and are not influenced by salivary flow rates (Kirschbaum & Hellhammer, 1992). Expected biological variance in cortisol includes distinct circadian rhythmicity (with peak

values at approximately 8:00 a.m. and nadir around midnight) and multiple ultradian

secretory bursts, in addition to environmental and situational reactivity (Baum &

Grunberg, 1995; Kuhn, 1989). However, unstimulated salivary cortisol measured at the

time of peak circadian levels and prior to appreciable environmental influences, that is,

immediately upon a.m. arising, have been shown to be consistent over sampling occasions

(Kirschbaum et al., 1990), with normal values of 11-15nmol/L (Kirschbaum &

Hellhammer, 1992). Salivette (Sarstedt) sampling kits were used for saliva specimen

collections. Cryopreserved cortisol and DHEA saliva specimens were batch-processed.

DHEA levels were measured by radioimmunoassay (Diagnostic Products Corporation)

and cortisol levels were measured by ELISA (Salimetrics) in the Core Laboratory of the

GCRC.

Lymphocyte subset assays were performed in the clinical Immune Monitoring

Laboratory under the direction of Dr. Pamela Kimball. To explore possible correlations

among helper/inducer and suppressor/cytotoxic T-lymphocytes with well-being among

persons with HIV disease, a number of lymphocyte subsets were examined in this study.

specifically CD4+, CD8+, CD57+, and CD8+/CD57+. These four were chosen because

CD4+ lymphocyte levels are a well established marker of HIV disease status and

progression, and CD8+, CD57+ and the combined subset of CD8+/CD57+ lymphocytes

may contribute information about cytotoxic immune cell functions. Although considered

an incomplete marker, because they only mark a portion of cytotoxic cells, the CD57+

subset is an enumerative measure of NK cells. Standard techniques for 2- color flow

cytometry were used (with Becton-Dickinson FACScan flow cytometer, FACScan

Research Software, and monoclonal antibodies) to identify the subsets of CD3+, CD4+, CD8+, and CD57+ lymphocytes.

All immune measures except lymphocyte subsets were done in the HIV Immunology Laboratory (established through a grant to Dr. Nancy McCain from the National Institute of Nursing Research), under the supervision of the Laboratory Director, Dr. Kevin Brigle. All specimens were cryopreserved and performed in batch runs to decrease inter-assay variability and control within-subject variability. Lymphocyte proliferation was to be measured by stimulating lymphocytes to divide in vitro in response to mitogens. Phytohemagglutinin (PHA) was the mitogen chosen because it is the most potent mitogen of those commonly used and is consistent with the work of Clerici and Shearer (1993, 1994). Mononuclear leukocytes were to be incubated first with control medium or medium with PHA and subsequently with tritiated thymidine. The amount of radioactivity incorporated by PHA-stimulated cells as compared to resting cells reflects the level of lymphocyte proliferation (Fletcher, Klimas, Morgan, & Gjerset, 1992). However, lymphocyte proliferation assays were not done. The newly standardized assay measuring lactic dehydrogenase release from lymphocytes did not perform reliably in our laboratory standardization procedures. The laboratory was not licensed to use the standard ^{3}thymidine assay.

Using previously cryopreserved mononuclear leukocytes, NK cell cytotoxicity was measured using a standard 4-hour chromium release assay with NK-sensitive K562 cells (American Type Culture collection) as targets. NK activity levels were reported as % lysis, calculated from the number of patient NK cells required to lyse 20% of the Cr-labeled

target cells. Thus, higher NK cytotoxic function is indicated by higher lytic units (Whiteside, Rinaldo, & Heberman, 1992).

In this study, standardized enzyme immunosorbent assay (ELISA) kits (Quantikine, R & D Systems) for cytokine quantification were used to examine peripheral blood levels of selected cytokines. To test the hypothesis that enhanced well-being is associated with a type 1 cytokine pattern, peripheral blood levels of IL-2 and TNF-alpha were measured to reflect a type 1 cytokine pattern and IL-4 and IL-6 were measured to represent a type 2 pattern.

Data Collection Procedures

Following enrollment and before the first treatment session, the participants turned in saliva samples collected that morning, completed the GWB, IES, POMS, HFIMS, and the Faces Scale and had serum 5-HT and immune measures drawn (Time 1). These measures were repeated after 4 weeks, at the completion of four HT sessions (Time 2). Additionally, the Faces Scale was completed immediately before and after each HT session and again 4 to 6 hours following the session. The investigator, with the assistance of a GCRC nurse, administered the psychosocial instruments to all participants. HT practitioners did not perform any data collection except pre-and post-treatment pulse measurements. Blood for measurement of the physiological variables was drawn by a nurse in the GCRC using standard universal precautions and aseptic technique.

Data Entry and Analysis

Creation and formatting of the database was done by the investigator. The psychometric data were scored by the investigator. All data were double-entered to verify

accuracy. Data were entered into a spreadsheet format with pretest, posttest, and control dependent variable data on the horizontal axis and participant ID code on the vertical axis.

Data were analyzed by the investigator using the SPSS 7.5 program. This statistical program allowed for data management, analysis, and presentation. Reliability of the well-being instruments was assessed using Cronbach's alpha as well as test-retest reliabilities using the wait-list control group data set. Construct validity was assessed among the measures of well-being. Baseline equivalence of the treatment and control groups was evaluated using stem and leaf plots to examine group differences on location, spread, and shape (Verran & Ferketich, 1987). The stated research questions of the study were tested in the form of null hypotheses using multivariate analysis of covariance (MANCOVA). MANCOVA allowed testing the difference among the means of two or more groups for two or more dependent variables simultaneously, while controlling for one or more covariates (Polit, 1996). Following multivariate analyses, univariate analysis of variance (UNIANOVA) was performed to assess the contribution of individual variables to the multivariate models. Additionally, correlational analyses were done to assess the relationships among the variables. The significance level for all statistical analyses was set at alpha = 05.

Conclusion

HT is a potentially beneficial therapy for individuals living with HIV disease. Research suggests it may indirectly enhance well-being. According to the PNI framework, psychological states influence physiological functioning. PNI is the study of the interactions between the brain and neuroendocrine and immune systems. Because it is difficult to measure directly the potential energetic effects of HT, indirect measures of

integrated psychological and physiological functioning are used currently to assess its efficacy. For these reasons, PNI was used as the framework for this clinical trial investigating the effects of HT in HIV-seropositive males. The majority of research to date on energy-based therapies is flawed methodologically making it difficult to advocate incorporation of these therapies into mainstream nursing care. This clinical trial was designed to provide adequate scientific rigor for investigating the effects of HT on well-being and neuroendocrine and immune measures in individuals living with HIV disease. This study contributes to the growing body of research in PNI as well as energy-based therapies. These results do not support the use of HT as it was administered in this study. Further research is needed before decisions can be make regarding the use of HT in HIV care.

Chapter 4

Findings

The purpose of this randomized clinical trial was to evaluate the effects of the

energy therapy HT on well-being and neuroendocrine and immune function in individuals

living with HIV disease. A total of 30 males were enrolled in the study between February

and April, 1999. A total of 27 individuals completed the study; one participant was lost to

follow-up and two participants withdrew following enrollment, but prior to starting the

intervention. Recruitment continued for five months, but efforts to replace these

individuals were unsuccessful. Of the 27 participants completing the study, 22 received

four 30-minute HT sessions and 5 received three 30-minute HT sessions. These five

individuals missed one treatment session and timely attempts at rescheduling were

unsuccessful. The pre-established protocol allowed participants to miss one session and

remain in the study.

Demographic Data

The demographic data indicated the study sample was similar to the local HIV

population, except no women were included in this clinical trial. There were no

statistically significant differences in the treatment and wait-list control groups on any of

the study variables at baseline. The mean age was 41 years (range 21 to 53, $\underline{SD}$= 7.53);

52% of the participants were African American ($\underline{n}$=14) and 48% were Caucasian ($\underline{n}$=13).

The mean number of years of education was 14 (range 6 to 21, $\underline{SD}$= 3.92). A total of 59%

of participants ($\underline{n}$=16) were single, 19% ($\underline{n}$=5) were married, and 22% ($\underline{n}$=6) were

divorced or separated. According to the CDC classification system, 33% ($\underline{n}$=9) of the

participants were Category A, indicating they were asymptomatic; 41% ($\underline{n}$=11) were

Category B, indicating they had experienced non-life threatening and/or non-AIDS

opportunistic illnesses; and 26% ($\underline{n}$=7) were Category C, meaning they had experienced

AIDS-defining conditions. The mean CD4+ lymphocyte count was 390 cells per microliter

or 24.2% of T-lymphocytes, with a range from 5.6% to 47.3% ($\underline{SD}$= 11.62). The average

rHCMSS symptomatology score was 19 (range 0 to 35, $\underline{SD}$= 13.5). Of the 27

participants, 23 were taking protease inhibitors. Of the remaining four participants, two

had never been placed on antiviral medications, one was taking ddI and d4T, and one was

taking only AZT because of multiple medication intolerances including protease inhibitors.

Two participants had only salivary measures because pre-baseline CD4+ lymphocyte

counts were less than 50 cells per microliter, which prohibited collecting serum samples.

Missing Data

Following completion of the study, approximately 4% of the data were missing,

virtually all because of participant non-response. The investigator also erred in not

collecting pulse measures on seven participants and occasionally missed administering

immediate pre- or post-treatment Faces Scales. With the exception of the pulse

measurements, the pattern for missing data was random. The majority of the participant

non-response missing data were the Faces Scales that should have been completed by

participants at home 4 to 6 hours following treatment. These Faces Scales were given to

participants in a packet to be completed following each weekly HT session. They were to

be mailed to the investigator following the final HT session. However, only 16 of 27 participants returned these instruments.

The decision was made to replace data because in MANCOVA cases are deleted listwise, meaning that if a participant is missing any variable included in the model, all of the participant's data are deleted from the analysis. Missing data were replaced when no more than 30% of the data were missing on any particular variable for a given participant. Using the most conservative approach, missing data were replaced with a participant's appropriate matched score. For example, if a pretest score was missing, the individual's posttest score was substituted so that no change was introduced. Therefore, conservatively replacing the data enabled a larger sample size for analysis, but a given participant's outcome was not affected. Although this approach potentially introduces a substantial conservative bias, the group's mean score was not used because of the relatively high variance in the data.

Instrument Evaluation

Reliability of four of the five well-being instruments was evaluated using Cronbach's alpha as well as test-retest correlations using control group data. Because the Faces Scale is a single-item measure, it was assessed using only test-retest reliability. The desired instrument reliability score = .70. As shown in Table 1, with the exception of the IES, which demonstrated low test-retest reliability, all of the instruments were internally consistent and stable measures of well-being in this sample.

Table 1

Well-being Instruments: Reliability Data

	Cronbach's alpha	Test-retest correlation
General Well-being Schedule (GWB)	.90	.70
Faces Scale		.71
Profile of Mood States (POMS)	.69	.70
Human Field Image Metaphor Scale (HFIMS)	.92	.90
Impact of Events Scale (IES)	.85	.54

The correlation matrix illustrating the Pearson correlations for the five measures at baseline is presented as Table 2. Construct validity was demonstrated through discriminant and convergent validity. The instruments reflecting positive well-being (GWB, Faces Scale, and HFIMS) were negatively correlated with those instruments reflecting psychological distress (POMS and IES). Additionally, the instruments were positively correlated with each other within the aforementioned groupings.

Table 2

Instrument Correlations (Significance Level) at Baseline

	GWB (n=27)	FACES (n=22)	POMS (n=27)	HFIMS (n=27)	IES (n=27)
GWB	1.00				
FACES	.50 (p=.017)	1.00			
POMS	-.72 (p<.001)	-.67 (p=.001)	1.00		
HFIMS	.26	.45 (p=.038)	-.38 (p=.048)	1.00	
IES	-.15	-.32	.35	-.28	1.00

Hypothesis Testing

Specific research hypotheses were that HT would (1) enhance well-being, (2)

increase levels of serum serotonin and salivary DHEA, (3) decrease levels of salivary

cortisol, and (4) enhance immune function in persons with HIV disease. The effects of HT

were first assessed using multivariate analysis of covariance (MANCOVA). Because of

the small sample size, three separate multivariate models were created. The first model

was comprised of the psychosocial measures (GWB, Faces Scale, POMS, HFIMS, and

IES). The second model contained the physiological variables (pulse; serotonin; DHEA;

cortisol; CD4+, CD8+, CD57+, and CD8+/CD57+ lymphocyte subsets; and NK

cytotoxicity). The third model contained the cytokines (IL-2, TNF-alpha, IL-4, and IL-6). In addition to the small sample size, the cytokines were placed in a separate model because they were the most tentative measures of immune function. To explore further the relationships among the variables in this study and to guide further univariate analyses to investigate the significant multivariate physiological findings, correlational analyses were done (Table 9). Because of the small sample size of the physiological variables, non-parametric Spearman's correlations were used. Following analysis of the multivariate models, exploratory analyses were done using univariate analysis of covariance (UNIANOVA). Baseline CD4+ levels and rHCMSS scores were the covariates used in all of the multivariate and univariate statistical analyses. Finally, to further evaluate the findings in this study, pre- and post-intervention means and standard deviations were examined to explore trends in the data.

Multivariate Psychosocial Model

Hypothesis 1. It was hypothesized that HT would enhance participant well-being. According to the multivariate statistical test, there were no measurable differences in well-being in the treatment group following HT as compared to the wait-list control group (Table 3). There was a significant time effect, which indicated both groups changed over time. There was not a significant interaction effect for group by time. Because of the significant time effect in the multivariate model, each variable was assessed using univariate analysis of variance (UNIANOVA) to identify the differences that contributed to this finding. However, there were no statistically significant findings in the univariate analyses.

Table 3

Mutivariate Analysis of Covariance: Psychosocial Model

Effect	Wilk's Lambda (df)	p
Group	.60 (6,12)	.03
Time	.42 (6,14)	.31
Group by Time	.65 (6,14)	.33

There were three univariate tests conducted on the Faces Scale data. The Faces Scale was completed by participants (1) before beginning and following completion of the 4-week HT intervention. Additionally, this scale was completed (2) immediately before and after each HT session as well as (3) 4 to 6 hours following each HT session. The post-intervention Faces Scale was the only well-being measure to approach a statistically significant change, with a trend toward higher scores at time 2 for both the treatment and control groups ($p=.06$). Pre- and post-intervention mean scores and comparative analyses for all psychosocial variables are presented in Table 4. Finally, although no significant change in well-being was detected following HT, there were trends in the mean scores of each of the instruments in the expected directions post-intervention; scores on the GWB, Faces Scale, and HFIMS increased and scores on the POMS and IES declined.

Table 4

Psychosocial Variables: Mean Scores and UNIANOVA

	Group	Mean	SD	F (df)	p
GWB (Range 14-124)	Treatment	Pre 64.79	13.61	1.27 (1)	.275
		Post 69.80	5.74		
	Wait-List Control	Pre 74.38	6.34		
		Post 69.75	7.40		
		Pre 69.41	11.62		
	Total Sample	Post 69.46	6.47		
Faces Scale (Range 1-7)	Treatment	Immed Pre 5.19	.93 .95	.250 (1)	.623
		Immed Post 5.80	1.38	.016 (1)	.902
		4-6 Hr. Post (w/Immed Post) 5.59	1.38 1.36	4.08 (1)	.062
	Wait-List Control	Pre 5.42	1.75		
		Post 6.00	1.15 1.59		
	Total Sample	Pre 4.69	1.24		
		Post 6.00			
		Pre 5.04			
		Post 6.00			
HFIMS (Range 25-125)	Treatment	Pre 65.79	21.12	.529 (1)	.477
		Post 70.89	23.74		
	Wait-List Control	Pre 55.69	21.10		
		Post 60.69	23.41		
		Pre 60.93	21.12		
	Total Sample	Post 65.98	23.74		
POMS (Range 0-68)	Treatment	Pre 12.71	10.15	.238 (1)	.632
		Post 10.43	7.98		
	Wait-List Control	Pre 13.31	10.64		
		Post 9.85	8.45		
		Pre 13.00	10.15		
	Total Sample	Post 10.15	7.98		
IES (Range 0-75)	Treatment	Pre 15.21	13.26	.120 (1)	.733
		Post 11.64	9.25		
	Wait-List Control	Pre 21.70	16.50		
		Post 18.46	19.47		
		Pre 18.33	14.98		
	Total Sample	Post 14.92	15.16		

<u>Multivariate Physiological Model</u>

    <u>Hypotheses 2, 3, 4</u>. Because hypothesis 4 was related to overall immune function, it was included here as well as the following cytokine multivariate model. It was hypothesized that HT would increase levels of serum serotonin and salivary DHEA, decrease salivary cortisol, and enhance immune function in individuals living with HIV disease. In the multivariate physiological model there was a significant treatment effect (Table 5). Additionally, like the psychosocial model, there was a significant time effect, meaning both groups changed over time. However, there was not a significant group by time interaction effect, which indicated the presence of a treatment effect independent of a time effect. It must be noted that although there was a significant treatment effect, the small sample size rendered the analyses unstable.

Table 5

<u>Multivariate Analysis of Covariance: Physiological Model</u>

Effect	Wilk's Lambda (df)	p
Group	.00 (9,2)	.001
Time	.03 (6,7)	.01
Group By Time	.33 (9,4)	.59

    Because of this significant multivariate effect, each variable was evaluated using UNIANOVA to detect which variables contributed to the overall multivariate effect. None

of the physiological variables demonstrated significant univariate results when tested individually (Table 6).

Trends in the mean scores and standard deviations of the variables were examined (Table 6). There was a modest decrease in the serum serotonin levels post-intervention in the treatment group. There was a slight post-intervention downward trend in CD8+ lymphocytes levels in both the treatment and control groups. Although not statistically significant, there was evidence of positive trends in the enumerative and functional indicators of NK cells. Specifically, upward trends were observed in NK cell cytotoxicity and there was no evidence of downward trends in CD57+ or CD8+/CD57+ levels in the treatment group. The absence of comparative data on the cytokines prohibits examination of trends in the data.

The final physiological variable in the multivariate model was pulse rate, which was assessed in 21 of the participants (the first treatment group did not have pulse measures because the investigator neglected to instruct the practitioners to do so). Although not statistically significant, there was a downward trend in mean pulse rates post-intervention. However, it must be noted the decreases could have been associated with rest alone because participants were lying down during their 20-30 minute session.

Table 6

Physiological Variables: Mean Scores and UNIANOVA

Measure	Group	Mean	SD	f (df)	p
Serotonin (ng/ml)	Treatment	Pre 80 00	66 10	452 (1)	511
		Post 73 62	65 79		
	Wait-list Control	Pre 91 33	76 77		
		Post 96 67	97 00		
	Total Sample	Pre 85 44	70 14		
		Post 84 68	81 33		
DHEA (ng/ml)	Treatment	Pre 1 58	70	3 65 (1)	074
		Post 1 59	49		
	Wait-list Control	Pre 1 56	91		
		Post 1 67	83		
	Total Sample	Pre 1 57	79		
		Post 1 63	67		
Cortisol (μg/dl)	Treatment	Pre 25	41	748 (1)	400
		Post 24	41		
	Wait-list Control	Pre 46	50		
		Post 58	45		
	Total Sample	Pre 38	41		
		Post 41	38		
CD4+ (%)	Treatment	Pre 24 40	13 28	063 (1)	804
		Post 21 10	13 48		
	Wait-list Control	Pre 24 02	10 48		
		Post 18 03	10 03		
	Total Sample	Pre 24 20	11 62		
		Post 19 49	11 66		
CD8+ (%)	Treatment	Pre 56 00	14 35	330 (1)	573
		Post 52 66	13 40		
	Wait-list Control	Pre 54 38	17 21		
		Post 51 72	13 28		
	Total Sample	Pre 55 44	15 59		
		Post 52 17	13 06		
CD57+ (%)	Treatment	Pre 24 95	12 27	1 22 (1)	284
		Post 24 71	10 37		
	Wait-list Control	Pre 23 11	8 85		
		Post 29 57	8 96		
	Total Sample	Pre 23 99	10 41		
		Post 27 24	9 78		
CD8+/CD57+ (%)	Treatment	Pre 22 46	11 33	094 (1)	763
		Post 21 93	10 17		
	Wait-list Control	Pre 18 90	8 10		
		Post 23 98	9 36		
	Total Sample	Pre 20 60	9 72		
		Post 22 68	9 58		
NK Cytotoxicity (lytic units)	Treatment	Pre 5 31	3 18	148 (1)	706
		Post 6 37	5 19		
	Wait-list Control	Pre 8 24	10 19		
		Post 6 73	5 10		
	Total Sample	Pre 6 64	7 21		
		Post 6 56	5 04		
Pulse (beats/min)	Treatment	Pre 87 00	8 31	407 (1)	532
		Post 80 01	9 71		

Multivariate Cytokine Model

Hypothesis 4. It was hypothesized that enhanced immune function would be demonstrated by a predominant type 1 instead of type 2 cytokine pattern in the treatment group following HT. However, there were no statistically significant findings in the cytokine multivariate model (Table 7).

Table 7

Multivariate Analysis of Covariance: Cytokines

Effect	Wilk's Lambda (df)	p
Group	.71 (4,7)	.60
Time	.61 (4,9)	.29
Group By Time	.70 (4,9)	.47

For continuity within the data analysis procedures and to provide directions for future research, univariate analyses were done on each of the four cytokines; none of these results were significant (Table 8). Because of problems with dilution techniques in the cytokine assays, data on group means and standard deviation scores are not reported. Intra-individual comparisons are valid, however.

Table 8

Cytokines: UNIANOVA

Cytokines	$\underline{F}$ $(\underline{df})$	$\underline{p}$
IL-2 (Type 1)	.92 (1)	.35
TNF-α (Type 1)	.19 (1)	.67
IL-4 (Type 2)	.26 (1)	.62
IL-6 (Type 2)	.530 (1)	.53

Exploratory correlational analyses were done to assess further the relationships among the study variables (Table 9; significant correlations are noted with asterisks). There were no significant correlations between the scores on the well-being instruments and the physiological measures. However, a number of significant correlations were found among the physiological measures. There were no significant correlations found for serotonin, DHEA, cortisol, or IL-4. Among the significant correlations, some were logical and explicable, whereas others were not. As expected the subset of CD4+ helper lymphocytes was correlated negatively with CD8+ suppressor lymphocytes and the mixed subset CD8+/CD57+. Similarly, CD8+, CD57+, and CD8+/CD57+ were correlated positively. NK cytotoxicity was correlated positively with CD4+ lymphocytes and inversely with the CD57+ and CD8+/CD57+subsets. The type 1 cytokines IL-2 and TNF-α were correlated positively. Both IL-2 and TNF-α were correlated postively with IL-6, perhaps indicating a type 0 cytokine pattern. The correlations among the various lymphocyte subsets and cytokines may be explained by the fact that each cell subset produces multiple cytokines.

Further exploratory univariate analyses were done by controlling baseline values of a variety of the physiological variables as covariates. These models were constructed based on the Spearman's correlational analyses as well as prior research. The only significant model (p= .03) was for a decrease in post-intervention salivary cortisol while controlling for baseline cortisol, DHEA, CD4+ lymphocyte percentage, and the rHCMSS symptomatology score.

Table 9

Correlational Analyses: All Psychosocial and Physiological Variables

	CD4+	CD57+	CD8+	CD8+/ CD57+	Cort	DHEA	IL-2	IL-4	NKcyto	Sero	TNF	IL-6
CD4+	1.00											
CD57+	-.33	1.00										
CD8+	-.55**	.55**	1.00									
CD8+/ CD57+	-.32	.94**	.67**	1.00								
Cort	.22	.02	.13	.057	1.00							
DHEA	.02	.10	.12	.047	-.04	1.00						
IL-2	.28	-.47*	-.40	-.52*	-.00	-.04	1.00					
IL-4	-.19	-.27	.06	-.22	-.21	.27	.10	1.00				
NKcyto	.53*	-.49*	-.43	-.50	.25	.10	.59**	.13	1.00			
Sero	.01	-.27	.04	-.30	-.15	.18	.28	.38	.40	1.00		
TNF	.32	-.15	-.45*	-.31	-.37	.18	.56*	-.12	.39	.26	1.00	
IL-6	.37	-.40	-.66**	-.59**	-.05	-.02	.66**	-.26	.36	.07	.59**	1.00
Faces	-.17	.01	.01	-.03	-.06	.08	.34	-.10	.15	-.02	-.15	.14
GWB	.16	-.10	.17	.03	.40*	-.05	.19	.20	.21	.04	-.08	.08
HFIMS	-.09	.04	-.02	.05	-.30	.08	.13	-.07	-.13	-.03	.20	-.07
POMS	.03	.01	.12	.12	.07	-.01	-.17	.32	-.11	-.14	-.03	.16
IES	-.16	.02	.07	-.01	-.01	.04	-.27	.05	-.15	.10	.17	.09

Note: * $p=.05$ ** $p=.01$

Summary

Using a multivariate analysis approach with univariate models constructed for specific explorations, it was found that HT did not enhance well-being and neuroendocrine and immune function as measured in this sample of individuals living with HIV disease. There was a statistically significant treatment effect detected in the multivariate physiological model, but there were no significant univariate findings to explain these results. Additionally, the small sample size rendered the results unstable. There was a significant decrease in cortisol when controlling for baseline levels of cortisol, CD4+

lymphocyte percentage, and rHCMSS symptomatology scores. Discussion and

conclusions related to the findings follow.

Chapter 5

Discussion and Conclusions

The PNI paradigm provided a holistic framework for examining interactions among well-being and the neuroendocrine and immune systems. This framework is particularly applicable in immunologically mediated diseases such as HIV disease. Using an experimental design and numerous controls, this clinical trial included the first global indicators of well-being in PNI/HIV research. Study hypotheses related to the effect of HT on well-being, neuroendocrine, and immune function in individuals living with HIV disease were rejected. While the overall multivariate physiological model was significant, differences in the individual variables were not significant. The findings did not support treatment-related changes with the exception of decreased cortisol when critical covariates were controlled. Although there were no other significant changes in the physiological variables, the multivariate physiological model was statistically significant, most likely because of additive effects of variables increasing or decreasing in the expected directions. There was a significant time effect in both the psychosocial and physiological models.

According to the multivariate analyses, both the treatment and control groups changed over time. This may have occurred because of the Hawthorne effect, or simply because participants were happy to be participating in the study. This time-related change in well-being and physiological status may have existed even with the control group because of a placebo response related to participants being hopeful that HT would help

them. Additionally, participants may have been happy they were receiving money for participating in the study. It is also conceivable that participants were affected by the caring presence of the investigator, HT practitioners, and GCRC staff. It is a common observation in nursing research that there is a therapeutic effect related to the nurse's use of self in nursing interactions. The investigator was aware of this potential effect and acknowledged the ultimate importance of therapeutic, humanistic interactions while attempting to maintain a professional, objective relationship with participants.

Explanations for the absence of a treatment effect are numerous and include the following: (1) the treatment did not work, (2) the treatment "dose" was insufficient to produce measurable changes in the chosen PNI-based parameters, (3) a "standardized" HT intervention may not be effective, (4) there was a ceiling effect related to the baseline level of participant well-being and immune function, (5) small sample size, and (6) the PNI-based measures chosen may not have been sensitive enough to detect small effect sizes. It is must be acknowledged that HT as it was delivered in this study did not appear to affect well-being and immune function in these individuals living with HIV disease.

Based on prior research, HT sessions were designed to maximize treatment effects. It is unlikely that the absence of a treatment effect was related to the HT practitioners because all of the practitioners had adequate, similar levels of training and practice experience. Although practitioners were given a 20-30 minute range for treatments, virtually all of the participants received 30-minute HT sessions. In clinical practice situations, HT sessions typically last 1 hour. Perhaps the duration of the session was not

long enough. Additionally, it is conceivable that changes related to HT are appreciated over time and were not detectable in the short 4-week course of this study. Qualitative explorations provide contextually grounded information for theoretical consideration when interpreting quantitative data in similar samples as well as directions for future research. Samarel (1992), following interviews with 20 individuals who had received TT, reported that TT was experienced as a multidimensional process that fostered personal growth and well-being over an extended time. Although this study involved substantially longer and more frequent HT sessions than prior studies, it is conceivable that significant changes are more effectively appreciated over longer periods of time.

There may have been a ceiling effect related to the participants' baseline well-being levels and immune function. The baseline scores on the psychosocial instruments were relatively high for the measures of well-being (GWB, Faces Scale, HFIMS) and relatively low for the two measures of psychological distress (POMS, IES). The participants in this study were relatively young and healthy. The mean age was 41 years, the average rHCMSS symptomatology score was19 with a range of 0 to 35, and the average CD4+ lymphocyte count was 390 cells per microliter. Further, the majority of the participants (23 of 27) were taking protease inhibitors (PI). Of the remaining four participants, two had never needed antiretroviral medications, one had never required PI, and one needed a combination of antiretrovirals but was unable to tolerate medications other than AZT. In responsive patients, current drug therapy including PI reduces viral load often to undetectable levels and increases CD4+ lymphocyte counts thereby decreasing morbidity and mortality, which potentially enhances well-being.

Because of the impact on the power of an intervention to demonstrate statistically significant changes, the small sample size and missing data likely contributed to the findings. Larger sample sizes are needed to achieve adequate power and stabilize variance in the statistical tests. Finally, the PNI-based measures chosen in this study may not have been robust enough to detect small effect sizes.

Well-being

With the exception of the test-retest reliability of the IES, the five psychosocial instruments used in this study were found to be reliable and valid indicators of aspects of well-being and psychological distress. Although there was no significant change in well-being post-intervention, there were trends in the expected directions in the post-intervention mean scores on each of the well-being instruments, in that scores on the GWB, Faces Scale, HFIMS increased and scores on the POMS and IES declined. The increase in the post-intervention Faces Scale scores approached a significant level (p=.06). The Faces Scale may have been the most sensitive measure because it is the simplest, most direct subjective measure of well-being. Hurny and colleagues (1996) advocated the use of single-item measures when assessing subjective states such as well-being and found that they often performed better than multi-item well-being instruments. The IES is an event-specific measure and the only one that had been used previously in the HIV population, but it was not a stable measure in this sample. However, because it measures psychological distress in the past 7 days, there is no reason to expect that distress levels remain stable from week-to-week.

Findings related to depressed mood and immune function in persons with HIV disease have included decreased lymphocyte proliferation to mitogens (Futterman et al.,

1994; Kemeny et al., 1994), decreased NK cell activity (Futterman et al., 1994), and alterations in WBC subpopulations (Taylor, 1995) in depressed individuals. According to the literature, negative life situations such as poor health are correlated negatively with well-being (Larson, 1978; Brook et al., 1979). Additionally, individuals "labeled" with a chronic illness can exhibit decreased well-being (Monk, 1981). Clearly the theoretical bases of the proposed hypotheses were sound. However, the study participants demonstrated relatively high baseline levels of well-being and receiving HT, as it was delivered in this study, did not enhance levels of well-being.

Neuroendocrine Measures

Serotonin. HT did not elicit significant changes in serum serotonin levels; the possible mechanisms are unclear, but include the absence of a treatment effect (which is consistent with the absence of significant changes in the other physiological variables), incorrect theoretical propositions about the function of serotonin within the PNI framework, and inappropriate measurement protocols.

A great deal remains unknown about the use of serum serotonin as a marker of neuroendocrine status in general and in individuals living with HIV disease in particular. Based on prior research, it was hypothesized that an enhancement in well-being would be associated with an increased amount of circulating serotonin and, subsequently, this increase in serotonin should augment immune function. However, there was no statistically significant increase in pre- to post-treatment serum serotonin levels in this sample. In fact, there was a trend toward a decrease in the serum serotonin levels post-intervention in the treatment group.

There have been no prior published studies measuring serum serotonin as a marker of neuroendocrine function in the absence of neuroendocrine disease states such as carcinoid. There is evidence that serotonin levels in the central nervous system fluctuate in response to moods, but no studies were located on mood and serum serotonin levels. There also is no literature on the appropriate time to measure serum serotonin levels. Perhaps changes in serum levels occur over a longer span of time than the 4-week interval in this trial. It is conceivable that changes occur not in serum levels, but in central receptor sites. Serum serotonin levels may remain relatively stable over time in the absence of neuroendocrine disease. Perhaps more importantly, sustained levels of well-being may be necessary to increase serum levels. The data indicate a downward trend in post-intervention levels. It is possible this finding correlates with an increase in receptor-laden serotonin or conceivably an increase in intersynaptic serotonin. Additionally, there is a wide normal range for serum levels (21-321ng/ml) making it more difficult to discern the physiological or clinical significance of changes. Finally, there is a vast variation in the levels intraindividually as well as across individuals. Perhaps serial levels are needed daily or weekly to ascertain significant changes.

DHEA and Cortisol. Although the multivariate physiological model was not statistically significant, the exploratory univariate model examining cortisol was significant while controlling for baseline cortisol, DHEA, CD4+ lymphocyte percentage, and rHCMSS score. Salivary cortisol levels declined in the treatment group and increased in the wait-list control group. There was no detectable change in DHEA levels post-intervention.

Measurement of salivary DHEA and cortisol is established in the literature. It is accepted that stress and negative affective states increase cortisol and decrease DHEA levels. No published reports were found concerning positive affective states and cortisol/DHEA levels. However, it was postulated that if negative affective states negatively impact this ratio, then positive affective states might have a positive impact, but these hypotheses were rejected.

In this study an ultrasensitive, standardized ELISA assay was used to measure cortisol, but the DHEA assay was the older radioimmunoassay. Perhaps the DHEA assay used was not sensitive enough to detect subtle changes. However, significant neuroendocrine changes would not be expected if those effects are predicated on significant changes in well-being. Perhaps perceived stress is a stronger correlate of cortisol and DHEA. Changes in well-being may be related to responses to stress but may not be sufficient to affect cortisol and DHEA levels.

Immune Measures

Lymphocyte subsets. Four lymphocyte subset measures were included in the statistical analysis, CD4+, CD8+, CD57+, and CD8+/CD57+ lymphocytes. There were no significant changes detected in lymphocyte subset percentages following HT. A downward trend was observed in CD4+ lymphocyte levels in both the treatment and wait-list control groups. There were similar downward trends in CD8+ lymphocyte levels in both groups. CD57+ and CD8+/CD57+ lymphocyte levels were the same pre-to post-intervention in the treatment group, but the control group demonstrated upward trends in this subset.

Acknowledging there is no treatment effect and given the trends in the data, perhaps HT does not increase CD4+ lymphocyte percentage, but conceivably attenuates

the disease-related decline over time. This is purely speculative because the data did not support a change in CD4+ lymphocyte levels post-intervention and participants were not assessed longitudinally. Although there was no detectable change in the percentage of CD8+/CD57+ cells, there was a trend toward higher NK cell cytotoxicity.

NK cytotoxicity. Although there is no significant change in the number of NK cells as HIV disease progresses, NK cells become functionally defective (Brenner, Dascal, & Wainberg 1989; Chehimi et al., 1992; Sirianni, Tagliaferri, & Aviti, 1990). In the univariate analysis, the change in pre- to post-intervention NK cell cytotoxicity approached significance ($p= .06$). This trend is consistent with the assertion that functional immune measures may be more sensitive than enumerative measures to psychosocial factors (Kiecolt-Glaser & Glaser, 1992; Schulz & Schulz, 1992).

Cytokines. Clerici and Shearer (1993, 1994) proposed that a type 1 cytokine pattern enhances cellular immunity whereas a type 2 pattern diminishes cellular immunity and enhances humoral immunity. These researchers acknowledged that their theory does not take into account interactions among all cell types in a dynamic system. The complex nature of the cytokine system makes it a challenge to measure changes in cellular production of cytokines. With this small data set, there is no clear demarcation of type 1 and type 2 cytokine patterns. There is essentially a type 0 pattern, indicating more normal immune function in these HIV-seropositive individuals than originally anticipated. Cytokines were the most promising, yet complicated and tenuous measures of immune system function in this analysis.

Pulse. Because energy therapies are theorized to elicit the relaxation response, pulse was measured before and after each treatment as an indirect measure of the

relaxation response. Participants were allowed at least 5 minutes to rest prior to pulse assessment. Although not statistically significant, there was a downward trend in mean pulse rates post-intervention. However, it must be noted the decreases could have been associated with rest alone because participants were lying down during their 30-minute HT session.

In summary, there were no significant changes in well-being or neuroendocrine and immune function following HT as it was delivered in this study. The theoretical basis for the research hypotheses were sound. Explanations for rejecting the proposed hypotheses include the true absence of a treatment effect, ceiling effects, inadequate treatment "dose," small sample size, and inadequate sensitivity of the chosen PNI-based measures. Based on the results of this study, implications, strengths and limitations, and directions for future research are offered.

<u>Implications</u>

As evidenced by the findings of this study, assessing the effectiveness of HT and applying the results when making clinical decisions remains a challenge. This was a rigorous scientific investigation into the effects of HT. It was specifically proposed that HT had the potential to improve well-being, thereby eliciting favorable changes in the neuroendocrine environment and ultimately enhancing immune function. Despite positive results in the literature, all of the study hypotheses were rejected.

Prior research involving energy therapies and PNI has produced some positive results, however many of the prior studies lacked adequate scientific rigor. This study was theoretically and methodologically sound and contributes significantly to the growing body of research in the area of energy therapies as well as PNI. The findings of this and

previous studies indicate there is a need for additional well-designed studies to further assess the efficacy of HT, which is increasingly being used in clinical practice.

Despite the limited statistically significant findings, each of the participants voiced only positive comments about the HT treatments they received. Further evidence of the participants' positive perceptions of the experience of receiving HT was the development of a bi-monthly HT program for participants who requested continued HT treatments, which started in October, 1999 at a community service agency. Independent of these findings, one of the HT practitioners who participated in the study established this program with two of the other practitioners now participating as well as one of the study participants who now helps schedule participants.

Strengths and Limitations

The major strengths of this study included its holistic approach based on a PNI theoretical framework and its experimental investigation of the increasingly popular complementary therapy of HT. There have been no reports of well-designed experimental trials on the effects of HT arising from a PNI paradigm. The psychosocial and physiological measures were grounded solidly in the PNI framework, both theoretically and empirically. The wait-list design was both ethically and scientifically sound, allowing treatment of all participants and comparing the influences of a short-term, cost-effective therapy on the subjective well-being and immune function of individuals living with HIV disease. As recommended by Herbert and Cohen (1993) multiple indicators of immune function were included to increase the reliability of the characterization of the participants' physiological environment and, subsequently, the understanding of relationships among affective, neuroendocrine, and immune parameters.

The most significant limitation was the small sample size. A larger sample size would have increased power and stabilized variance in the statistical analyses. Despite the short duration of this study, attrition was a known threat. There were three enrolled participants who did not complete the study. Although this is a small number, given a total sample size of 30, it was a notable level of attrition (10%). Individuals living with HIV disease have unstable immune systems and potentially are coping with complex issues which may make them more likely to withdraw from the study due to illness. Participant enrollment continued until a total of 30 participants had been enrolled. Recruitment efforts continued for 5 months but additional participants were not enrolled.

A second limitation involved the control of the HT intervention. The majority of the TT research presented in the literature review involved 5-minute TT interventions. The timing of the sessions in HT research has been more variable. Although practitioners were allowed 20-30 minutes for HT sessions in this study, this did not allow sufficient time for individualized treatment based on recipient needs. The intervention treatment time was less than the typical 45-60 minute sessions in actual practice. The 20-30 minute time restriction allowed the five HT practitioners to treat the necessary number of participants in a timely manner without excessive fatigue. Additionally, the same techniques were used with all participants. These restrictions were necessary to enhance scientific rigor but are not consistent with the usual practice of this therapy. While this restriction limited generalizability, such scientific control was necessary. Direct practice applications will require further research.

Finally, this clinical trial was not longitudinal. The hypotheses tested in this study involved the potential effects of HT on the neuroendocrine and immune environment in

individuals living with HIV disease over only 4 weeks. Even if the statistical hypotheses had not been rejected indicating there was a significant treatment effect, limited conclusions could be drawn regarding the clinical significance of such short-term changes in the study parameters.

Recommendations for Future Research

Adequate theoretical and empirical evidence supported this investigation of the effects of HT on well-being, serum serotonin levels, DHEA and cortisol, and immune function in individuals living with HIV disease. Research to date on energy therapies has yielded primarily positive results, although further study using more rigorous methods is warranted.

Recommendations for future research include well-designed experimental studies with adequate sample sizes. Consideration of effect size is imperative. Effect size can be increased with a larger sample size, more sensitive outcome measures, as well as considerations related to strengthening treatment effects including an increased "dose" of the intervention (increased frequency and longer duration of HT sessions). Additionally, when interpreting findings, data and conclusions must be congruent. Although it is appropriate to examine trends and draw inferences that contribute to understanding the data and developing future research, if there is no statistically significant treatment effect, conclusions are limited. Finally, despite prior evidence correlating affective states and immune function, it is still unclear whether there are significant implications for health outcomes in PNI-based studies. Longitudinal, outcome-based research is needed to assess the impact of mind-body therapies, including energy work, on the HIV disease trajectory.

Longitudinal research investigating the effects of HT is required to assess the long-term impact on disease progression.

Based on the findings of this study, specific recommendations can be made regarding the choice of outcome measures in future research. The Faces Scale is a valid and reliable measure of well-being. It is also easy to administer and score. The use of this scale should be considered in future investigations involving complementary therapies and well-being.

Despite the absence of a statistically significant physiological model in this clinical trial, there is substantial research to support continued exploration into neuroendocrine and immune dysfunction in HIV disease as well as interventions that potentially enhance immune function and impede HIV disease progression. Salivary measures of DHEA and cortisol are methodologically sound, cost effective, and non-invasive measures of neuroendocrine function and should be considered in future studies. Serum serotonin samples are complicated to process and expensive to assay. Until clearer evidence is available, this may not be a good indicator of changes in the neuroendocrine environment.

CD4+ lymphocyte levels are established as valid and reliable indicators of HIV disease status and progression and must be considered in studies involving individuals living with HIV disease, at least as covariates if not outcome measures. According to the literature, functional measures are as important as enumerative measures when assessing HIV disease progression. Research to date supports the use of lymphocyte proliferation and NK cytotoxicity as indicators of immune function in HIV disease (Clerici & Shearer, 1993, 1994; Lucey et al., 1991; Clerici, Roilides, & Butler, 1992; Brenner et al., 1989;

Clerici et al., 1989; Nott, 1995). Cytokine levels are costly and complicated to interpret in

a clinically meaningful way in the context of HIV disease. Nevertheless, cytokine

production is a promising measure of immune system function. There is substantial

research to support the indirect immunoendocrine dialogue between cortisol and cytokines

and the progression of HIV disease (Norbiato et al., 1997; DeKruyff, Fang, & Umetsu,

1997; Blotta, Dekruyff, & Umetsu, 1997).

Finally, research is needed to foster understanding of how individuals living with

HIV disease appraise the significance of their experiences, including the effects on their

daily lives as well as their long-term goals and aspirations. Well-designed qualitative

research will provide information about the experience of living with HIV disease and

provide directions for formulating future research questions and designs. Additionally,

qualitative explorations into the experience of giving and receiving HT may provide

knowledge about specific outcome measures, which is imperative because the mechanisms

of action of energy therapies remain poorly understood.

Conclusion

This was a well-designed interventional study of the effects of HT on well-being

and neuroendocrine and immune function in 27 males living with HIV disease, yet all of

the research hypotheses were rejected. Possible explanations for the lack of a treatment

effect include that HT did not work, the lack of statistical power to detect a treatment

effect related in part to a small sample size, and a high level of participant well-being at

baseline, among others. Although there was no detectable enhancement of well-being and

neuroendocrine and immune function in the participants in this study, there was no

indication of harm and participants perceived positive benefits while receiving HT. The

potential impact of positive affective states on well-being has remained largely unexplored. This research contributes to the developing knowledge base of energy therapies. These results do not support the use of HT in HIV care. Further research is need before the decision can be made regarding the therapeutic use of HT in HIV care.

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Crown
Forehead
Throat
Heart
Solar plexus
Sacral
Base
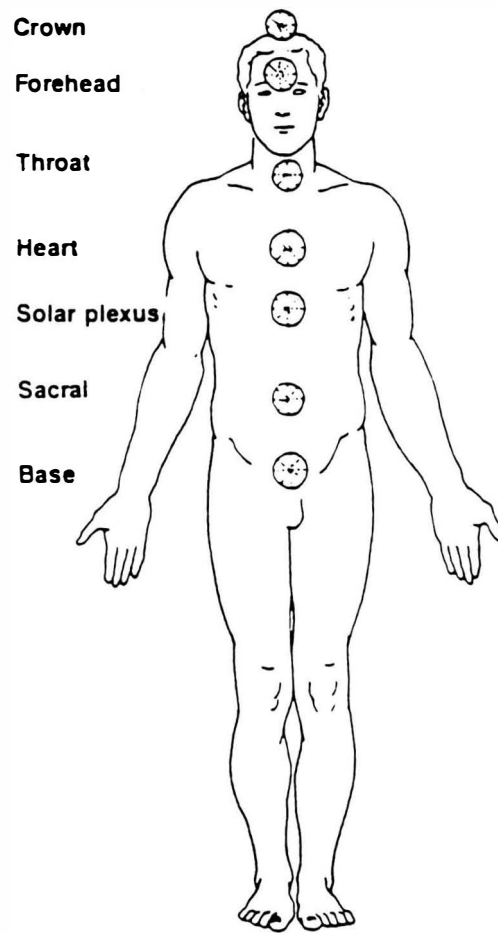
A. The seven major chakras

Brennan, B.A. (1987). <u>Hands of light: a guide to healing through the human energy field</u>. New York: Bantam Books

APPENDIX A: PHYSIOLOGIC CONNECTIONS AND THE MAJOR CHAKRAS

CHAKRA	ENDOCRINE GLAND	AREA OF BODY GOVERNED
• 1-Base	Adrenals	Spinal column, kidneys
• 2-Sacral	Gonads	Reproductive system
• 3-Solar Plexus	Pancreas	Stomach, liver, GB, PNS
• 4-Heart	Thymus	Heart/circ.system, vagus nerve
• 5-Throat	Thyroid	Throat, Pulm. and GI
• 6-Head	Pituitary	Lower brain, L eye, ears, nose, nervous system
• 7-Crown	Pineal	Upper brain, R eye

Adapted from Brennan, B.A. (1987). Hands of light: A guide to healing through the human energy field. New York: Bantam Books

APPENDIX B:
CHAKRA CONNECTION TECHNIQUE

Mentgen, J. & Bulbrook, M. (1995). Healing touch level II notebook (pp. 98-102).
Carrboro: North Carolina Center for Healing Touch

CHAKRA CONNECTION

#1

#2

#3

#4

APPENDICES

CHAKRA CONNECTION

#5

#6

#7

#8

CHAKRA CONNECTION

#9

#10

#11

#12

CHAKRA CONNECTION

#13

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#16

CHAKRA CONNECTION
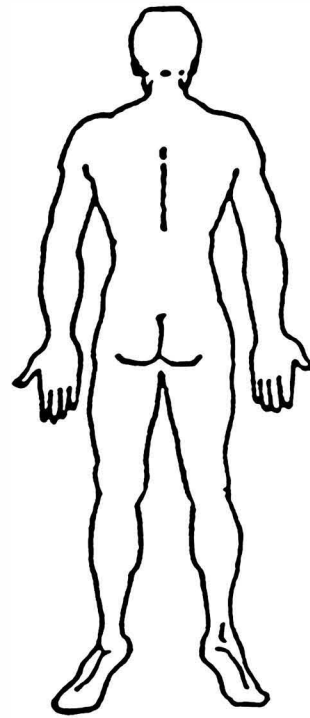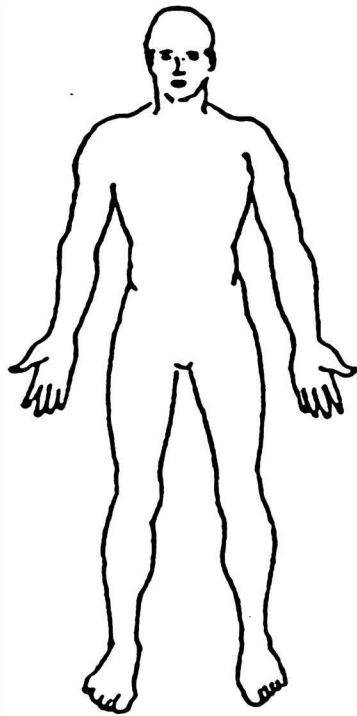
#17

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#20

102

Client:_____

Date:_____Session #:_____

ASSESSMENT/ FINDINGS:

ENERGY TREATMENT/ FINDINGS:

APPENDIX C:

- **Data Record Form**
- **CDC Classification Form**
- **Revised HIV Center Medical Staging Scale**
- **Karnofsky Performance Index**
- **Cognitive Capacity Screening Examination**

Date of enrollment _____/_____/_____   GROUP _____ ID CODE _____

Name _____   Contact Telephone _____

Mailing Address _____

▪▪

Recruitment Source _____   GROUP _____ ID CODE _____

DATA RECORD:

KARNOFSKY (≥ 60) _____ COGNITIVE EXAM (≥ 20) _____ rHCMSS _____ CDC CLASS _____
      Attachment 1   Attachment 2   Attachment 3   Attachment 4

AGE=____ YEARS of EDUCATION=____   RACE: 1=Black. 2=Hispanic. 3=White. 4=Other _____

PARTNER STATUS: 1=Single, never married; 2=Married or Life Partner; 3=Divorced or Separated; 4=Widowed

DATE OF FIRST-KNOWN HIV-INFECTED DIAGNOSIS _____   PRE-BASE CD4: (≥50 within 3 months FOR BLOOD)
                                               Date _____ Count _____ % _____

USUAL WEIGHT (i.e., normal weight prior to
       illness-related weight loss) _____

RISK FACTORS: ALCOHOL USE:

    1. Blood   5. Combination 1 and 2   1. None or rarely
    2. Homosexual/bisexual   6. Combination 1 and 3   2. ≤ 3 drinks/week
    3. Heterosexual   7. Combination 1 and 4   3. ≤ 2 drinks/day
    4. Injection   8. Combination 2 and 4   4. ≥ 3 drinks/day
                           9. Combination 3 and 4   5. Binging (i.e., excessive intake
                                                           that occurs in irregular pattern)
                                                           6. #5 + consistent pattern of intake

CURRENT MEDICATIONS: (No steroids, immunomodulators)   PSYCHOTROPIC DRUGS (Prescribed):
    Start date of **current Rx** _____   (Descriptive) _____
    Circle all that apply: _____
    0. None   5. 3TC (Epivir)   PSYCHOACTIVE DRUG USE (Illicit):
    1. AZT (Retrovir)   6. Nevirapine   (Descriptive) _____
    2. ddC (HIVID)   7. Protease Inhibitor   _____
    3. ddI (Videx)   (ALSO code 1-6,8)   FREQUENCY OF USE:
    4. d4T (Zerit/Stavudine)   8. Other _____   1. None or rarely
                                                                   2. ≤ 3 times/week
                                                                  3. Daily

USE OF COMPLEMENTARY/ALTERNATIVE THERAPIES (Descriptive) _____
_____

EXERCISE PATTERN:
(Descriptive) _____ [Occupational exercise may be coded as #2 or #3, depending on level of activity.]
    1. **Minimal**
    2. Sporadic, effortful
    3. Moderate aerobic (1 unit 3X/wk) (e.g., one aerobic "unit" = 20-minute cycling, 45-minute brisk walking, jogging < 3 miles)
    4. Routine aerobic (≥ 3 units/wk or conditioned intense) (e.g., jogging ≥ 3 miles, 5 times a week)
    5. Maximal aerobic or unconditioned intense (e.g., competitive running, cycling, weight training) (Not within 24 hours)

1993 Revised CDC Classification System for HIV Infection (CDC, 1992b)

CD4+ T-lymphocyte COUNT	CLINICAL CATEGORIES		
	(A) Asymptomatic, acute (primary) HIV or PGL*	(B) Symptomatic, not (A) or (C) conditions	(C) AIDS-indicator conditions
(1) ≥500/microliter	A1	B1	C1
(2) 200-499/µL	A2	B2	C2
(3) <200/µL	A3	B3	C3

Clinical Categories

Category A consists of one or more of the conditions listed below in an adult or adolescent (≥ 13) with documented HIV infection. Conditions listed in Categories B and C must not have occurred.

Asymptomatic HIV infection Persistent generalized lymphadenopathy
Acute (primary) HIV infection with accompanying illness or history of acute HIV infection

Category B consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical Category C and that meet at least one of the following criteria: (a) the conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or (b) the conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection. **Examples** of clinical conditions in category B include, **but are not limited to:**

Bacillary angiomatosis Candidiasis, oropharyngeal (thrush)
Hairy leukoplakia, oral Idiopathic thrombocytopenic purpura
Listeriosis Peripheral neuropathy
Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy
Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
Constitutional symptoms, such as fever (3 8.5C) or diarrhea lasting >1 month
Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome
Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess

For classification purposes. Category B conditions take precedence over those in Category A. For example. someone previously treated for oral or persistent vaginal candidiasis (and who has not developed a Category C disease), but who is now asymptomatic should be classified in clinical Category B.

Category C includes the clinical conditions listed in the AIDS surveillance case definition (listed below). For classification purposes, once a Category C condition has occurred, the person will remain in Category C.

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

Scoring Instructions: Based on history and physical examination data, but <u>independent of CDC classification and immune status</u>, derive a numerical score between 0 and 39 to categorize an individual's HIV-specific health status. **First**, categorize the individual by one of the major stages: Asymptomatic, Minor Symptoms, Major Symptoms, or AIDS. **Second**, categorize the severity of symptomatology within the designated stage by assigning a score from 0-9, 10-19, 20-29, or 30-39.
Note that scores are assigned for <u>any history</u> or <u>current evidence</u> of a given symptom: once a staging score has been assigned, it cannot decline on subsequent examinations. ANCHORED INDICATORS ARE APPROXIMATIONS ONLY: actual scores may include all integers and are based on clinical judgment.

Range	Stage: Description and Indicators

0-9   **Asymptomatic:** Physical symptoms may be attributed to HIV infection, but are not, in themselves, of clinical concern.

> 0 = No history of symptoms
>
> 5 = Minor fatigue (less than 25% reduction in normal activity)
>
> 9 = > usual URIs

10-19   **Minor Symptoms:** Limited, but clinically significant symptoms which are not included below (e.g., persistent generalized lymphadenopathy, oral or vulvovaginal candida, skin and nail infections or rashes, constitutional symptoms of limited duration, episodic diarrhea, fatigue with 25-50% reduction in normal activity, Cervical dysplasia [CIN 1-2]

> 10 = PGL
>
> 15 = ≤ 2 symptom episodes: List _____
>
> 19 = ≥ 3 symptom episodes: List _____

20-29   **Major Symptoms:** Serious physical symptoms, but not AIDS-defining conditions, including the following (check if applicable):

___ Oral hairy leukoplakia (OHL)	___ Night sweats > 30 days	___ Pelvic inflammatory disease (PID)
___ Salmonella septicemia (once)	___ Fever > 30 days	___ Cervical dysplasia (CIN 3)
___ Pneumococcal bacteremia	___ Diarrhea > 30 days	___ Peripheral neuropathy
___ H. influenza bacteremia	___ Fatigue > 30 days	___ Herpes zoster
___ Weight loss > 10% body wt	___ Idiopathic thrombocytopenia purpura (ITP)	

Other: _____

> 20 = ≤ 2 symptom episodes
>
> 25 = Recurrent major symptom episodes
>
> 29 = Chronic and/or multiple major symptom episodes

30-39   **AIDS:** Any AIDS-indicator condition, including the following (check if applicable):

___ Candidiasis, esophageal or pulmonary	___ Isosporiasis, chronic intestinal
___ Coccidioidomycosis	___ MAC, M. kansasii or other (ds, ep)
(disseminated [ds] or extrapulmonary [ep])	___ M. tuberculosis, any site
___ Cryptococcosis (ep)	___ Pneumocystis carinii pneumonia (PCP)
___ Cryptosporidiosis, chronic intestinal	___ Recurrent pneumonia
___ Cytomegalovirus (not liver, spleen, or nodes)	___ Progressive multifocal leukoencephalopathy
___ Encephalopathy	___ Recurrent Salmonella septicemia
___ Histoplasmosis (ds, ep)	___ Toxoplasmosis of brain
___ Herpes simplex	___ Wasting syndrome
(chronic, esophagus, pulmonary)	Malignancy, SPECIFY: __ KS __ lymphoma __ invasive cervical

> 30 = ≤ 2 AIDS-indicator illness episodes and/or conditions of limited severity
>
> 35 = Recurrent indicator conditions
>
> 39 = Chronic and/or multiple opportunistic infections

KARNOFSKY PERFORMANCE INDEX

DEFINITION	%	CRITERIA
Able to carry on normal activity and to work. No special care is needed.	100	Normal: no complaints: no evidence of disease
	90	Able to carry on normal activity; minor signs or symptoms of disease
	80	Normal activity with effort: some signs or symptoms of disease.
Unable to work. Able to live at home. care for most personal needs. but a varying amount of assistance is needed.	70	Cares for self. but unable to carry on normal activity or to do active work
	60	Requires occasional assistance. but is able to care for most personal needs
	⇓_____ = **Not eligible**	
	50	Requires considerable assistance and frequent medical care
Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly.	40	Disabled: requires special care and assistance
	30	Severely disabled: hospitalization is indicated although death not imminnent
	20	Very sick: hospitalization necessary; active supportive treatment necessary
	10	Moribund: fatal processes progressing rapidly
	0	Dead

Karnofsky, D.A.. Abelmann. W.H., Craver. L.F.. & Burchenal. J.H. (1948). The use of the nitrogen mustards in the palliative treatment of carcinoma. Cancer. 1, 634-656.

DATA RECORD ATTACHMENT 4
COGNITIVE CAPACITY SCREENING EXAMINATION

Instructions: Check items answered correctly. Write incorrect or unusual answers in space provided. If necessary, urge patient once to complete task. Introduction to patient: "I would like to ask you a few questions. Some you will find very easy and others may be very hard. Just do your best."

USE CLINICAL JUDGMENT TO ASSESS: (RETURN TO THESE ITEMS IF SCORE < 20 OR QUESTIONABLE.)
1) What day of the week is this?
2) What month?
3) What day of month?
4) What year?
5) What place is this?
6) Repeat the numbers 8 7 2.
7) Say them backwards.
8) Repeat these numbers 6 3 7

BEGIN HERE WITH SPECIFIC ITEMS, UP TO TOTAL OF 20 POINTS:

9) Listen to these numbers 6 9 4. Count 1 through 10 out loud, then repeat 6 9 4. (Help if needed.)

10) Listen to these numbers 8 1 4 3. Count 1 through 10 out loud, then repeat 8 1 4 3.

11) Beginning with Sunday, say the days of the week backwards.

12) 9 − 3 is _____.

13) Add 6 (to the previous answer or "to 12").

14) Take away 5 ("from 18").

REPEAT THESE WORDS AFTER ME AND REMEMBER THEM. I will ask for them later: HAT, CAR, TREE, TWENTY-SIX.

15) The opposite of fast is slow. The opposite of up is _____.

16) The opposite of large is _____.

17) The opposite of hard is _____.

18) An orange and a banana are both fruits. Red and blue are both _____.

19) A penny and a dime are both _____.

20) What were those words I asked you to remember? (HAT)   (21) (CAR)
22) (TREE)   (23) (TWENTY-SIX)

24) Take away 7 from 100, then take away 7 from what is left and keep going: 100 - 7 is	**OR**	Spell WORLD backwards (interviewer spell W-O-R-L-D)
25) Minus 7 (26) Minus 7		Score 1 point for each letter:
27) Minus 7 (28) Minus 7		(24) D (26) R
29) Minus 7 (30) Minus 7		(25) L (27) O
		(28) W

EACH ITEM COUNTS AS ONE POINT: TOTAL CORRECT MUST BE GREATER THAN 19. (Maximum score = 30)

Jacobs et al. (1977). Annals of Internal Medicine, 86, 40-46.

APPENDIX D:

GENERAL WELL-BEING SCHEDULE

McDowell, I. & Newell, C. (1996). Measuring health: A guide to rating scales and questionnaires, 2nd ed. New York: Oxford University Press

These are questions about how you feel and how things have been going with you. For each questions. mark (X) beside the answer which best applies to you.

1.   How have you been feeling in general? (during the past month)

_____ 1.   In excellent spirits
_____ 2.   In very good spirits
_____ 3.   In good spirits mostly
_____ 4.   I have been up and down in spirits alot
_____ 5.   In low spirits mostly
_____ 6.   In very low spirits

2.   Have you been bothered by nervousness or your "nerves"? (during the past month)

_____ 1.   Extremely so--to the point where I could not work or take care of things
_____ 2.   Very much so
_____ 3.   Quite a bit
_____ 4.   Some-enough to bother me
_____ 5.   A little
_____ 6.   Not at all

3.   Have you been in firm control of your behavior. thoughts. emotions. OR feelings? (during the past month)

_____ 1.   Yes. definitely so
_____ 2.   Yes. for the most part
_____ 3.   Generally so
_____ 4.   Not too well
_____ 5.   No, I am somewhat disturbed
_____ 6.   No, I am very disturbed

4.   Have you felt so sa d. discouraged, hopeless, or had so many problems that you wondered if anything was worthwhile? (during the past month)

_____ 1.   Extremely so--to the point that I have just about given up
_____ 2.   Very much so
_____ 3.   Quite a bit
_____ 4.   Some--enough to bother me
_____ 5.   A little bit
_____ 6.   Not at all

5.	Have you been under or felt you were under any strain, stress, or pressure? (during the past month)	
	_____	1. Yes--almost more that I could bear or stand
	_____	2. Yes--quite a bit of pressure
	_____	3. Yes--some, more than usual
	_____	4. Yes--some, but about usual
	_____	5. Yes--a little
	_____	6. Not at all
6.	How happy, satisfied, or pleased have you been with your personal life? (during the past month)	
	_____	1. Extremely happy--could not have been more satisfied or pleased
	_____	2. Very happy
	_____	3. Fairly happy
	_____	4. Satisfied--pleased
	_____	5. Somewhat dissatisfied
	_____	6. Very dissatisfied
7.	Have you have any reason to wonder if you were losing your mind, or losing control over the way you act, talk, think, feel, or of your memory? (during the past month)	
	_____	1. Not at all
	_____	2. Only a little
	_____	3. Some--but not enough to be concerned or worried about
	_____	4. Some and I have been a little concerned
	_____	5. Some and I am quite concerned
	_____	6. Yes, very much so and I am very concerned
8.	Have you been anxious, worried, or upset? (during the past month)	
	_____	1. Extremely so--to the point of being sick or almost sick
	_____	2. Very much so
	_____	3. Quite a bit
	_____	4. Some--enough to bother me
	_____	5. A little bit
	_____	6. Not at all
9.	Have you been waking up fresh, and rested? (during the past month)	
	_____	1. Every day
	_____	2. Most every day
	_____	3. Fairly often
	_____	4. Less than half the time
	_____	5. Rarely
	_____	6. None of the time

10. Have you been bothered by any illness, bodily disorder, pains, or fears about your health? (during the past month)

    _____ 1. All the time
    _____ 2. Most of the time
    _____ 3. A good bit of the time
    _____ 4. Some of the time
    _____ 5. A little of the time
    _____ 6. None of the time

11. Has your daily life been full of things that were interesting to you? (during the past month)

    _____ 1. All the time
    _____ 2. Most of the time
    _____ 3. A good bit of the time
    _____ 4. Some of the time
    _____ 5. A little of the time
    _____ 6. None of the time

12. Have you felt down-hearted and blue? (during the past month)

    _____ 1. All the time
    _____ 2. Most of the time
    _____ 3. A good bit of the time
    _____ 4. Some of the time
    _____ 5. A little of the time
    _____ 6. None of the time

13. Have you been feeling emotionally stable and sure of yourself? (during the past month)

    _____ 1. All the time
    _____ 2. Most of the time
    _____ 3. A good bit of the time
    _____ 4. Some of the time
    _____ 5. A little of the time
    _____ 6. None of the time

14. Have you felt tired, worn out, used-up, or exhausted? (during the past month)

    _____ 1. All the time
    _____ 2. Most of the time
    _____ 3. A good bit of the time
    _____ 4. Some of the time
    _____ 5. A little of the time
    _____ 6. None of the time

For each of the four scales below, note that the words at each end of the 0 to 10 scale describe opposite feelings. Circle any number along the bar which seems closest to how you generally felt during the past month.

15.　How concerned or worried about your HEALTH have you been? (during the past month)

```
0    1    2    3    4    5    6    7    8    9    10
!    !    !    !    !    !    !    !    !    !    !
```

Not   Very
concerned   concerned
at all

16.　How RELAXED or TENSE has you been? (during the past month)

```
0    1    2    3    4    5    6    7    8    9    10
!    !    !    !    !    !    !    !    !    !    !
```

Very   Very
  relaxed   tense

17.　How much ENERGY. PEP. VITALITY have you felt? (during the past month)

```
0    1    2    3    4    5    6    7    8    9    10
!    !    !    !    !    !    !    !    !    !    !
```

No energy   Very
AT ALL,   ENERGETIC.
listless   dynamic
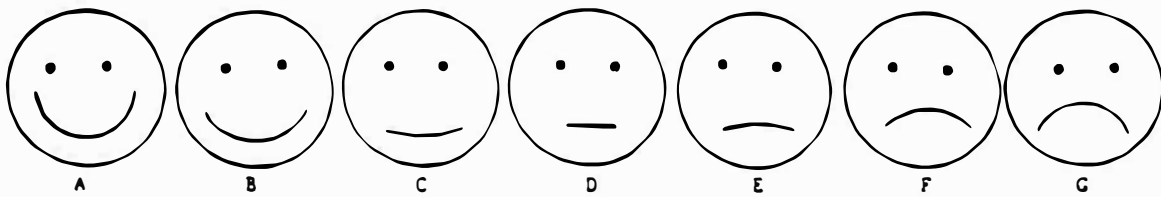
18.　How DEPRESSED or CHEERFUL have you been? (during the past month)

```
0    1    2    3    4    5    6    7    8    9    10
!    !    !    !    !    !    !    !    !    !    !
```

Very   Very
depressed   cheerful

Andrews, F. & Withey, S. (1976). Social indicators of well-being. New York: Plenum

Please read each of the following metaphors and indicate how you feel at the moment. Check the box that best describes how you identify with each statement. If you do not identify with the statement, check the box under, "do not identify". If you identify strongly with the statement, check the box under "strongly identify". There are no right or wrong answers.

I Feel ...	Do Not Identify	Slightly Identify	Moderately Identify	Strongly Identify	Totally Identify
1. free as a bird.					
2. one with the universe.					
3. like an eternal song.					
4. like a melody.					
5. like a tree in winter.					
6. like a fenced in yard.					
7. like a symphony.					
8. like a ray of light.					
9. like a bird in a cage.					
10. like an ocean breeze.					
11. like a kite with no wind.					
12. one with the world.					
13. like a ray of hope.					
14. like a worn out shoe.					
15. like I can touch the stars.					
16. like a fragrance on the wind.					
17. like I'm standing on the highest mountain.					
18. like ripples on a pond.					
19. like a free spirit.					
20. like a new pair of skates					
21. like a tree in springtime.					
22. like a garden in spring.					
23. like an artist with a brush					
24. like I can see forever.					
25. like my hands are tied.					

APPENDIX D
Brief Poms

Below is a list of words that describe feelings people have. Please circle the number that best describes how you have been feeling during the past week, including today.

		Not At All	A Little	Moderately	Quite A Bit	Extremely
1.	Unhappy	0	1	2	3	4
2.	Energetic	0	1	2	3	4
3.	Sad	0	1	2	3	4
4.	On Edge	0	1	2	3	4
5.	Carefree	0	1	2	3	4
6.	Blue	0	1	2	3	4
7.	Uneasy	0	1	2	3	4
8.	Cheerful	0	1	2	3	4
9.	Discouraged	0	1	2	3	4
10.	Miserable	0	1	2	3	4
11.	Relaxed	0	1	2	3	4
12.	Muddled	0	1	2	3	4
13.	Gloomy	0	1	2	3	4
14.	Alert	0	1	2	3	4
15.	Weary	0	1	2	3	4
16.	Bewildered	0	1	2	3	4
17.	Ready to fight my illness	0	1	2	3	4

IMPACT OF EVENT SCALE

Below is a list of comments made by people with HIV-infection or AIDS. Please check the appropriate column to indicate how frequently these comments were **true for you** during the past **7 days.** If they did not occur during that time, please mark the "not at all" column.

	Not at All	Rarely	Sometimes	Often
1. I thought about it when I didn't mean to.				
2. I avoided letting myself get upset when I thought about it or was reminded of it.				
3. I tried to remove it from memory.				
4. I had trouble falling asleep or staying asleep, because of pictures or thoughts about it that came into my mind.				
5. I had waves of strong feelings about it.				
6. I had dreams about it.				
7. I stayed away from reminders about it.				
8. I felt as if it hadn't happened or it wasn't real.				
9. I tried not to talk about it.				
10. Pictures about it popped into my mind.				
11. Other things kept making me think about it.				
12. I was aware that I still had a lot of feelings about it, but I didn't deal with them.				
13. I tried not to think about it.				
14. Any reminder brought back feelings about it.				
15. My feelings about it were kind of numb.				

APPENDIX E:
CONSENT FORM/Research Information Sheet
Dissertation Title: Healing Touch in HIV Disease
Principle Investigators: Nancy L. McCain, RN, DSN
Jo L. Wheeler Robins, RN, MS, ANP
Faculty Advisor: Nancy L. McCain, RN, DSN
Medical College of Virginia Hospitals/Virginia Commonwealth University

You are being invited to participate in a research study on the influences of healing touch in persons with HIV infection. If you decide to participate, you will be one of 30 people who will be involved in this study. The study is designed to examine the effects of healing touch on well-being, selected immune-related hormones, and several blood tests of immune system function.

Healing touch is a therapy based on the idea that the human body is made up of energy and that imbalances or blockages in the flow of that energy can impair health and well-being. Energy based therapies have been shown to increase well-being and they may also enhance immune system functioning. The healing touch session will last 20-30 minutes and will involve a nurse experienced in healing touch lightly placing her hands on specific areas of the body that correspond with the theorized major energy centers of the body. Your participation also will help us to understand the influence of well-being on the immune system in HIV disease, and we may be able to provide better health care in the future. The only known risks or discomfort involved in this research are the brief pain of a needle-stick when having blood drawn from an arm vein, and the very slight chance of local infection at the site of the needle stick. Sterile procedures will be used to minimize the risk of such infection.

If you decide to participate in this study, you will be involved for at least 4 weeks. In a random manner similar to the toss of a coin, you will be assigned (1) to the healing touch group or (2) to a wait list group to begin the study 4 weeks later. The healing touch treatment will involve 30-minute healing touch sessions once a week for 4 weeks.

Research data will be collected at the beginning and end of the treatment group. If you are assigned to wait for the intervention, you will also have data collected at the beginning and

end of the wait list period. Data collection will require about 30 minutes of your time and will involve having lab work drawn and completing a set of four brief questionnaires. Additionally, you will be asked to collect saliva samples the morning of data collection. At the 4-week data collection time, you will be paid $50. You will not be paid or allowed to continue in the study if you miss two of the healing touch sessions or a data collection time.

In the event of physical and/or mental injury resulting from your participation in this research project, Virginia Commonwealth University will not provide compensation. If injury occurs, medical treatment will be available at the Medical College of Virginia Hospitals. Fees for such treatment will be billed to you or to appropriate third party insurance.

Your participation is entirely voluntary, and you may decide not to participate or to withdraw from the study without fear of disruption of the usual care, attention, or commitment of any of your health care or social services providers. Your participation and the information obtained will be kept strictly confidential, and it will not be possible to identify any participant from the reports or publications that may result from this research. You may ask questions now or at any time you wish in the future by contacting Jo Wheeler at ████████ or Nancy McCain at ████████ If you have any questions concerning your rights as a research subject, you may contact the Committee on the Conduct of Human Research at ████████ for information or assistance.

Your initials here indicate that you understand the nature and requirements for your participation in this research study, that you voluntarily agree to participate in the study as outlined here and verbally explained to you, and that you have received a copy of this form.

_____   YOUR INITIALS ONLY_____
Researcher's Signature

Date: _____

Participant I.D.	IL-2		TNF-α	IL-4	IL-6
Treatment Group 02	Pre Post	24 1141	979 3491	1.3 8.4	16829 25213
04	Pre Post	902 491	2197 1904	269 31.6	11290 14746
06	Pre Post	884 1853	3531 4322		46765 45573
08	Pre Post	353 879	901 2691	21.4 50.7	27076 4235
12	Pre Post	78 7	1991 223	30 2.9	275 67
13	Pre Post	5 362	<0.5 2715		8 48116
16	Pre Post	1007 934	5417 3481	3.3 1.2	37939 37818
18	Pre Post	1307 1353	3348 3030	2.6 7.4	37780 28974
22	Pre Post	463 326	5146	6.6	25574
24	Pre Post	22 13	1413 9452	1.8 1.7	655 22652
25	Pre Post	417 302			
27	Pre Post	59 38	1523 725	5.9	15553 9640
Control Group 01	Pre Post	283 1293	2908 4760	5.1 8.2	38420 35764
03	Pre Post	1435 431	1841 2516	15.7	35427 510

05	Pre	39	2676	<0.25	31221
	Post	79	1260	5.1	3134
07	Pre	1051	2149	3.3	35130
	Post	1115			
09	Pre	325	1557	62.1	14920
	Post	1033	2404	195	3123
11	Pre	148	893		36825
	Post	158	1307	15	39147
14	Pre	18			
	Post	459	3060		58202
15	Pre	893	2475	9.8	85565
	Post	449	2396	16.4	59999
17	Pre	1714	2324	4.8	52738
	Post	13	862	65.7	471
19	Pre				
	Post	810	3983	3.3	48045
21	Pre	167	2825	24	34548
	Post	444	3369	17.5	19588
28	Pre				
	Post	44	1832		19943