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**EFFECTS OF RELAXATION TRAINING ON PHYSIOLOGICAL
AND PSYCHOLOGICAL MEASURES OF DISTRESS AND QUALITY
OF LIFE IN HIV-SEROPOSITIVE SUBJECTS**

DISSERTATION

**Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University**

By

Sharon Stout-Shaffer, M.S., R.N.

*** * * * ***

**The Ohio State University
1999**

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ABSTRACT

Immunosuppressed populations appear to be at particular risk for health changes associated with the stress of chronic illness. Thus, the purpose of this study was to examine the effect of relaxation on psychological, physiological, and behavioral measures of stress in an adult HIV-1+ population. Men and women were randomly assigned to undergo either a 12-week relaxation protocol consisting of autogenic and progressive muscle training and standard guided imagery techniques ($n = 18$) or served as wait list controls ($n = 11$). Practice was monitored through self-report and weekly practice logs. Outcome variables were theoretically based on a biobehavioral model of chronic illness and included (a) psychological distress (Profile of Mood), (b) quality of life (MOS-HIV), (c) salivary cortisol, (d) health behavior, and (e) CD4+/CD8+ ratio and viral load. Outcomes were assessed at baseline (week 2) and at weeks 6, 10, and 14, with the exception of CD4+ and CD8+ cell count and viral load assessments, which were collected weeks 2 and 14. Treatment-related improvements in quality of life were evident in role function and health transition as assessed on separate MOS-HIV subscales: a treatment by time interaction for Role Function [$F(2.3,81) = 4.2$; $p = .01$] and a treatment effect for Health Transition [$F(1,27) = 5.1$; $p < .05$]. Additionally, there were consistent indications suggesting a treatment-related reduction in

psychological distress on the POMS total mood and 6 POMS subscales that failed to reach significance. The treatment group's health behavior improved compared to controls [$F(2.5,81) = 4.7$; $p < .01$]. Post hoc analysis suggested that such benefits may be achieved after 4 weeks of relaxation practice. With regard to the physiologic measures, CD4+ cell counts improved, evidenced by a significant treatment by time effect [$F(1,25) = 4.6$; $p < .05$]; however, log-transformed data showed a significant difference between groups for viral load [$F(1,26) = 4.8$; $p < .05$]. No treatment-related changes were detected in the remaining physiologic measures. Anecdotally, relaxation was found useful for nine frequently reported symptoms, including fatigue and pain. These findings suggest that relaxation may facilitate the modification of several psychological, physiological, and behavioral manifestations of stress and increase quality of life in HIV-1+ adults who are compliant with medications and committed to practice.

Dedication

This study is dedicated to Daniel Neal Shaffer.

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To the subjects who participated in this research, thank you for allowing me to share in your healing journey.

From my father, Walther M. Stout, M.D., I learned of the courage and spirit required to live with debilitating chronic illness; from my mother, Mary R. Stout, R.N., I learned about the healing nature of love.

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CHAPTER 1

INTRODUCTION

Introduction

Human immunodeficiency virus (HIV-1) is a chronic immune system disease of significant social and economic importance. The Centers for Disease Control (1995) estimated that approximately 1.5 million people are infected with HIV in the United States and the nature of the epidemic is changing to include more women, adolescents, injection drug users, and racial/ethnic minorities. Worldwide infection rates have been estimated as 24 million for adults and 1.5 million for children (Quinn, 1996). The HIV-1 virus primarily attacks the T-lymphocyte helper/inducer cell (CD4+); however, other cellular immune components, such as T-lymphocyte suppressor/cytotoxic (CD8+) cells, natural killer cells (NK), and B-lymphocytes are also severely compromised (Calabrese, Kling, & Gold, 1987; Solomon, Kemeny, & Temoshok, 1991). In the United States and other western countries, recent advancements in antiretroviral and protease inhibitor drug therapy have increased the probability of survival, yet treatment regimens are costly, and infected individuals experience numerous social, financial, and personal stressors as well as secondary symptoms that reduce quality of life (Chesney & Folkman, 1994; Grassi et al., 1999; Kemeny, 1994a; Kemeny et al., 1989; Lenderking et al., 1994; McCain & Cella, 1995; McCain & Zeller, 1996). At a social-

economic level, the emergence of HIV-1 has led to extremely high direct costs for medical care and drug therapy, reduced economic output, and substantial indirect costs to society (Baum, Herberman, & Cohen, 1995; Quinn, 1996).

A diagnosis of HIV+ impacts all aspects of life (Hardy, 1996; Revicki, Wu, & Murray, 1995) and numerous studies have documented the acute and chronic nature of stress associated with the disease (Chesney & Folkman, 1994; Fawzy, Namir, & Wolcott, 1989; Holzemer & Wilson, 1995; Kemeny et al., 1989; Solomon et al., 1991). The nature of ongoing stress associated with diagnosis and treatment of life threatening chronic illness is related to high rates of psychological distress, depression, diminished quality of life, and alterations in neuroendocrine function that are thought to negatively impact immune function. Although the effects of prolonged psychosocial stress on overall health outcomes are less clear, studies suggest that negative affect, severe physical and financial stress, and a lack of social support are predictive of poorer medical outcome (Anderson, Kiecolt-Glaser, & Glaser, 1994; Chuang, Devins, Hunsley, & Gill, 1989; Kiecolt-Glaser & Glaser, 1991; Kiecolt-Glaser et al., 1985; McCain & Zeller, 1996).

Interventions such as relaxation have been shown to ameliorate stress induced autonomic, neuroendocrine, and cellular immune function, as well as lead to actual health changes such as a reduced risk of infection (Kiecolt-Glaser & Glaser, 1992, 1995; Maier, Watkins, & Fleshner, 1994; Spiegel & Moore, 1997). Relaxation therapy appears to influence the same neuroendocrine mechanisms activated during stress and has been suggested as an important area of research for HIV and other

immunosuppressed populations. However, documentation of possible long-term benefits of relaxation therapy on psychological, neuroendocrine, and immune function is sparse (Kiecolt-Glaser & Glaser, 1992, 1995).

Purpose

The purpose of this study was to examine changes in psychophysiological indicators of stress in HIV+ adults who regularly practiced relaxation. The intervention tested was a 12-week program of relaxation that incorporated guided imagery.

The study hypotheses were based on a biobehavioral model of adjustment to chronic stress, which posits that the psychological distress and reduced quality of life frequently associated with chronic illness negatively impact cellular immunity via neuroendocrine pathways and changes in health behavior, and that these biologic effects may influence long-term health outcomes (Anderson et al., 1994). The intervention tested was hypothesized to mitigate the adverse effects of chronic stress on these systems.

Study Hypotheses

1. In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in psychological distress.

2. In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in quality of life.

3. In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit a significant decrease in AM and PM salivary cortisol levels.

4. In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit a significant increase in the CD4+/CD8+ T-lymphocyte ratio and a significant decrease in viral load.

5. In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in health behavior.

Definitions of Terms

Chronic Stress. Living with the physiological, psychological, and social-economic consequences associated with chronic illness, specifically HIV (Anderson et al., 1994; Thompson, Nanni, & Levine, 1996). Salivary cortisol was the physiological measure of chronic stress.

Health Behavior. Consistent ability to meet an acceptable standard of behavior in the following areas: adherence to drug regimen, alcohol intake, aerobic exercise, nutritional intake, tobacco use, and sleep as measured by a Health Behavior checklist.

These behaviors have been shown to be susceptible to alterations under conditions of chronic stress and are known to influence immune function.

Psychological Distress. A state of negative emotional affect or mood as measured by the Profile of Mood State (POMS) total and subscale scores.

Quality of Life. A multidimensional construct that includes functional ability, psychological functioning, social adjustment, and disease and treatment-related symptoms (Anderson et al., 1994), as measured by the Medical Outcomes Survey HIV (Wu et al., 1991) and a General Symptom Checklist.

Relaxation. A physiological response resulting in consistent elevation of peripheral skin temperature and a self-rated experience of relaxation attained through practice of structured exercises that incorporate sensory imagery.

Significance

This study is significant for several reasons. First, it incorporated a biobehavioral model of stress to explore psychological, neuroendocrine, and health behaviors known to influence stress-immune reactivity and long-term health outcomes. Use of this model aligns the content with several other investigators exploring the relationships of chronic illness, stress, and disease outcomes. Second, a recent survey of 127 HIV+ subjects found that the use of complementary therapies, such as relaxation, exercise, and diet change, in the HIV+ population is dramatically increasing (Sabo, Paterson, & Carwein, 1996). Thus, ongoing research is important for documenting how and for whom these strategies are effective. Third, this is the only known relaxation

study to incorporate a practice requirement and use repeated measures to systematically document practice effects over time. Based on post hoc findings from previous studies, practice is an important variable for interpreting research outcomes. Finally, the specific intervention approached relaxation as a psychophysiological (mind-body) stress management tool. It incorporated use of standardized mental imagery to enhance physiological relaxation and to provide active, individualized coping strategies related to physical symptoms, emotions, and beliefs which may interfere with achieving physical relaxation.

CHAPTER 2

REVIEW OF LITERATURE

Introduction

Psychoneuroimmunology (PNI), an emerging field of study, examines the relationship of stress to specific psychological and behavioral variables, the autonomic nervous and neuroendocrine systems, and the immune system. This chapter describes the PNI model used to guide the study and reviews the literature related to major model constructs. Applications of the model to the study of HIV and relaxation therapy for HIV+ subjects are then reviewed.

Biobehavioral Model of Stress and Disease Course

The Biobehavioral Model, shown in Figure 1, was adopted for use in this study to reflect its application in HIV disease. The model was developed as a framework to organize the increasing body of PNI research in the cancer population (Anderson et al., 1994) and, as a research framework, has clear relevance for use in the study of other chronic illnesses, particularly those that involve a decrease in immune competence (McCain & Zeller, 1996).

Figure 1. Biobehavioral Model. A biobehavioral model of the psychological (stress & quality of life), behavioral (compliance & health behaviors), and biologic pathways from stressors to disease course. CNS = central nervous system/autonomic nervous system
From: Anderson, B., Kiecolt-Glaser, J., & Glaser, R. (1994).

The model proposes that diagnosis of a life-threatening illness (cancer) and initiation of treatment lead to emotional distress. Additionally, long-term treatment and the associated psychological, physiological, and social-economic disruptions lead to chronic stress and a reduced quality of life. The physiological mechanisms involved include (a) the autonomic nervous system and neuroendocrine pathway and (b) specific health behaviors known to influence immune function. A growing body of research shows that psychological distress, acute and chronic life stressors (negative events), and reduced quality of life are reliably associated with down-regulation of the immune system (Anderson et al., 1994; Calabrese et al., 1987; Herbert & Cohen, 1993a, 1993b; Kiecolt-Glaser & Glaser, 1991; Perry, Jacobsberg, Card, & Ashman, et al., 1993; Sgoutas-Emch et al., 1994; Shultz & Shultz, 1992; Solomon et al., 1991).

Cellular Immune Changes Associated with Acute and Chronic Stress

Human stress research has used naturalistic and laboratory stress models to document that acute stressors produce immunologic changes in relatively healthy individuals. Naturalistic stressors that have been studied include academic examination stress (Kiecolt-Glaser et al., 1986), diagnosis of cancer and anticipation of treatment (Bovbjerg et al., 1990), and anticipation of HIV test results (Antoni, Baggett et al., 1991; Antoni, Schneiderman et al., 1991). Common laboratory stressors include exposure to noise (Sieber, Rodin, & Larson, 1992; Weiss, Pato, McAllister et al., 1990), cognitive challenge (Bachen, Manuck, & Marland, 1992; Naliboff, Benton, & Solomon, 1991), and electric shock (Weiss et al., 1990). Recent meta-analysis of the acute stress literature shows that acute stress is consistently associated with an increased number of circulating natural killer (NK) cells, increased natural killer cell cytotoxicity (NKCC), a decrease in blastogenic response to Concanavalin (Con A) mitogen, an increased number of circulating T-lymphocyte suppressor (CD8+) cells, and decreased number of T-lymphocyte helper (CD4+) cells (Cacioppo et al., 1995; Kiecolt-Glaser, Cacioppo, Malarkey, & Glaser 1992; Kusnecov & Rabin, 1994). Data from animal studies vary somewhat, perhaps reflecting a time difference from application of the acute stressor to measurement of physiological parameters; however, both human and animal studies suggest that the changes seen reflect transient alteration in lymph migration or redistribution of leukocytes from blood to other body organs (Cacioppo

et al., 1995; Dhabhar & McEwen, 1997; Sgoutas-Emch et al., 1994). These reversible changes are thought to be immuno-enhancing (Dhabhar & McEwen, 1997).

Chronic stress, however, specifically under conditions of repeated psychological distress and low social support, is thought to be immuno-suppressive (Dhabhar & McEwen, 1997; Herbert & Cohen, 1993a, 1993b; Kiecolt-Glaser & Glaser, 1995; McEwen, 1998; Unicho, Cacioppo, & Kiecolt-Glaser, 1992). The body of human research under chronic stress conditions—such as bereavement (Herbert & Cohen, 1993a), depression (Herbert & Cohen 1993b), relationship failures and marital discord (Kiecolt-Glaser et al., 1987b), and caregiving for a relative with debilitating disease (Kiecolt-Glaser et al., 1987a)—suggests that long-term stress is associated with down-regulation of neuroendocrine function (Anderson et al., 1994; Cacioppo et al., 1995; Maier et al., 1994; Dhabhar & McEwen, 1997), as well as cell-mediated immune function (Dhabhar & McEwen, 1997). Additionally, long-term repeated exposure to stressors has been found to erode social support (Cacioppo, 1992; Cohen, Kaplan, Cunnick, Manuck, & Rabin, 1992) and affect brain function, especially in the hippocampus, which can lead to impairment in memory and feelings of fatigue, lack of energy, irritability, demoralization, and hostility (McEwen, 1998).

Recent meta-analyses of 44 human studies suggest that the specific effects of chronic stress on cellular immune function include a decrease in total lymphocyte count, a decrease in CD4+ and CD8+ lymphocytes as well as CD4+/CD8+ ratio, and a decrease in NK cell number and NKCC (Herbert & Cohen, 1993a, 1993b; O’Leary, 1990). Objective stressful events, such as bereavement and divorce, and other events

with interpersonal or social components are associated with greater immune alteration (NKCC) than are self-reports of stress, perceived stress, and non-social events (Herbert & Cohen, 1993a).

Physiological and Behavioral Mechanisms Associated with Stress and Immunity

The mechanisms by which stressful social and psychological processes and reduced quality of life affect cellular immune function are an ongoing focus of study. As shown in Figure 1, two major pathways have been hypothesized to influence immune reactivity to stress: physiological and behavioral (Anderson et al., 1994; Kiecolt-Glaser & Glaser, 1988, 1991; McEwen, 1998).

Physiological. The Autonomic Nervous System (ANS) and the Hypothalamic-Pituitary-Adrenal (HPA) neuroendocrine axis are two physiological pathways that have been implicated in reducing cellular immune function under conditions of chronic stress. The ANS is comprised of two major branches, the Sympathetic Nervous System (SNS) and the Parasympathetic Nervous System (PNS).

SNS activation releases catecholamines from nerves and the adrenal medulla, and HPA activation leads to secretion of adrenocorticotropin (ACTH) from the pituitary that in turn mediates the release of cortisol from the adrenal cortex. Both the ANS and HPA axis are adaptive systems that respond to stress by activation or “turning on” a complex adaptive pathway and inactivation or “shutting off” this response when the threat is past (allostatic response). Inactivation occurs through a negative feedback loop, so that the system returns to baseline levels of catecholamines and cortisol

(Calabrese et al., 1987; Daruna & Morgan, 1990; Dhabhar & McEwen, 1997; McEwen, 1998). Chronic stress is thought to be associated with maladaptation of allostatic systems, whereby a physiologic response either persists long after the stress has subsided or is activated repeatedly. Disruption of the circadian corticosterone in rats or cortisol rhythm in humans may be an indicator or mediator of maladaptation to chronic stress (Daruna & Morgan, 1990; Dhabhar & McEwen, 1997).

Recent evidence suggests that the ANS and HPA axis constitute a shared mechanism for situations of both acute and chronic stress. Individuals high in sympathetic reactivity respond with increased adrenocorticotrophic hormone (ACTH), cortisol, and immune changes compared to other groups. Thus, sympathetic reactivity may be a marker or determinant of individual immune response to stress, and individuals with high sympathetic reactivity may be more susceptible to the long-term changes seen with chronic stress (Cacioppo et al., 1995; Kiecolt-Glaser et al., 1995).

Long-term psychological distress and repeated environmental stressors can lead to failure of HPA axis and SNS negative feedback, increasing sympathetic reactivity and leading to physical overexposure to stress hormones, particularly cortisol (Cacioppo et al., 1995; Daruna & Morgan, 1990; McEwen, 1998). The immunosuppressive effects of elevated serum cortisol have been well documented (Calabrese et al., 1987; Daruna & Morgan, 1990; Dhabhar & McEwen, 1997; Kiecolt-Glaser et al., 1992; Kiecolt-Glaser & Glaser, 1991, 1995; Kolesnitchenko & Snart, 1992; Malarkey, Kiecolt-Glaser, Pearl, & Glaser, 1994; Kusnecov & Rabin, 1994; Unicho et al., 1992). Corticosteroids act by directly binding to CD4⁺ cells, the primary target in HIV

infection, and inhibiting T cell activation. Thus, glucocorticoids are responsible for depression of T-lymphocyte number, percent, and function (Calabrese et al., 1987; Daruna & Morgan, 1990; Dhabhar & McEwen, 1997; Herbert & Cohen, 1993b) and may be a major inducer of CD4+ cell death (Idziorek, Baert, Herman, & Dewulf, 1998).

Behavioral. Distressed individuals are frequently prone to behaviors that are known to directly or indirectly affect immune reactivity to stress (Anderson et al., 1994). Anxious and depressed individuals are more likely to self-medicate. Alcohol intake, tobacco use, and drug use have been found to positively correlate with depressed immune function (Kiecolt-Glaser & Glaser, 1988).

The effects of chronic stress may also be exacerbated by poor nutrition and reduced by moderate exercise (Kiecolt-Glaser & Glaser, 1988; McEwen, 1998; Zeller, McCain, McCann, Swanson, & Colletti, 1996). Appetite disturbance and poor nutrition have been associated with impairment of cell-mediated immunity (Chandra, 1982). Similarly, data have accumulated to suggest that exercise may buffer psychological distress, particularly anxiety and depression, and modify the cardiovascular and immuno-suppressive effects of chronic stress (Dubert, 1992; LaPerriere et al., 1994; MacArthur, Levine, & Birk, 1993; MacVicar, Winningham, & Nickel, 1989; Rigsby, Dishman, Jackson, Maclean, & Raven, 1992). However, for patients with chronic illness, adequate exercise maintenance may be difficult to achieve, and frequency of other symptoms such as nausea, vomiting, and fatigue make it difficult to mobilize the resources needed to maintain positive health behavior (Anderson et al., 1994; Maier et al., 1994; McCain & Cella, 1995). Finally, quality of life factors, such as increased

disability, increased frequency of symptoms, and duration of treatment, correlate with behavioral noncompliance to the treatment regimen (Anderson et al., 1994; Holzemer et al., 1999).

Clearly, consideration of health behaviors is important for any PNI research, and quantitative data on these factors should be obtained from all subjects for use in statistical analysis (Anderson et al., 1994; Kiecolt-Glaser & Glaser, 1988, 1991; McCain & Zeller, 1996; Zeller, McCain, McCann et al., 1996). How health behavior and neuroendocrine functions interact to influence immune responses to stress and the implications for health promotion remains to be elucidated (Kiecolt-Glaser & Glaser, 1988, 1992; McCain & Smith, 1994).

HIV, Stress, and Quality of Life

Living with a diagnosis of HIV+ has much in common with the acute and chronic stress conditions that are known to depress immune competence. One recent study underscored the acute stress associated with diagnosis of HIV+. Ironson et al. (1990) assessed 36 at-risk men taking the HIV-1 antibody test and 25 controls who did not undergo testing. Those who tested HIV+ reported significantly more anxiety and traumatic stress compared to those who tested HIV- or those who were not tested. Among the HIV+ group only, significant negative correlations ($r = -.69$) were found between self-reported anxiety measured at the time of notification and NKCC measured one week later.

Other recent studies point to the chronic nature of stress experienced by HIV+ individuals, characterized by repeated exposure to a high number of objective stressors, high levels of emotional and psychosocial distress, and reduced quality of life (Calantino, 1997; Chuang et al., 1989; Lenderking et al., 1994; LaPerriere et al., 1994; McCain & Cella, 1995; Nott & Vedhara, 1995; Siegel & Krauss, 1991; Solomon et al., 1991; Thompson et al., 1996; Turner & Lloyd, 1995). Furthermore, psychological distress and depression appears to occur at early points in the progression of HIV disease (Chuang et al., 1989). Major adaptive challenges required to deal with the stressors of this chronic illness have been described as dealing with a curtailed lifespan, dealing with social reactions to a stigmatizing illness, and developing strategies to maintain physical and emotional health (Siegel & Krauss, 1991).

While the nature of chronic stress has been reported, relationships among psychological distress, immunological status, and disease progression have been less well defined and reports have been mixed (Burack et al., 1993; Kemeny et al., 1989; Lyketsos et al., 1993; McCain & Cella, 1995; Perry & Fishman, 1993; Rabkin et al., 1991). In a correlational study of 53 men with HIV disease, McCain and Cella (1995) differentiated negative stress levels from positive stress levels by use of a modified 11-item version of the POMS (Brief TMDS). Negative stress was defined as stress associated with negative affect or distress, and positive stress was defined as stress associated with positive affect, i.e., acquiring new coping skills. Meaningful correlations were found between negative stress levels and lower quality of life ($r = .64$), more avoidant and intrusive thinking ($r = -.56$), and more mood disturbance

($r = -.58$). The hypothesized relationships between negative stress level and lower CD4+ counts and percentages were not found. Lower CD4+ cell counts were correlated with increased positive stress ($r = -.43$); however, there were no meaningful correlations between stress and CD4+ percentages or CD4+/CD8+ ratio. The authors noted that circadian variations in CD4+ counts were not controlled for in this correlational study. In a separate study of 62 HIV+ men, Goodkin, Fuchs, Feaster, Leeka, and Rishel (1992) found a strong relationship between higher number of life stressors coupled with a passive coping style, and lower total lymphocyte and CD4+ counts.

For the past 7 years, Kemeny and colleagues at the University of California, Los Angeles, have been investigating whether psychological processes could function as cofactors and contribute to disease progression in HIV+ individuals. One study compared 90 HIV+ and HIV- gay men who had lost one or more friends in the prior year to a sample matched for age and serostatus (Kemeny et al., 1989). Among HIV+ subjects, depressed mood in bereaved men was not associated with immune parameters; however, in nonbereaved men, depressed mood was strongly associated with lower CD4+ cell percentages, higher percentages of CD8+ T-lymphocytes, and lower lymphocyte proliferation responses, a pattern prognostic for the development of AIDS. In the HIV- group, depressed mood (in bereaved subjects only) was associated with lower NK cell counts. In a second study, chronically depressed HIV+ subjects showed a steeper decline in CD4+ T-lymphocytes levels over a 5-year period than did non-depressed men matched for age and baseline CD4+ levels (Kemeny et al., 1994). Long-

term data from the UCLA study team document that depression in non-bereaved subjects, negative HIV-specific expectancies, and lack of engagement with important life goals appear to be associated with a pattern of immune changes prognostic for the development of Acquired Immune Deficiency Syndrome (Cole, Kemeny, & Taylor, 1997; Solomon et al., 1991). A recent study of 45 HIV+ bereaved men followed for 3 years showed that men who engage in active cognitive coping after loss were more likely to find meaning and purpose for the loss. Furthermore, men who found meaning showed significantly less rapid declines in CD4+ T-lymphocyte cell ratio and significantly less AIDS mortality, independent of baseline health or health behavior (Bower, Kemeny, Taylor, & Fahey, 1998).

The San Francisco Men's Health Study supported the suggestion that psychological depression influences immune function for HIV+ subjects. Burack et al. (1993) found that, among 772 HIV-infected gay men without AIDS followed for 5 years, depression was significantly related to decline in CD4+ T-lymphocytes. Those classified as affectively depressed had a 34% greater mean annual rate of decline in CD4+ counts when controlling for known baseline physiological predictors of HIV progression, such as antiretroviral drug regimen, alcohol use, and recreational drug use. Although depressed subjects had a 10% higher death rate, depression was not significantly related to earlier AIDS onset or earlier mortality. Reports from this group argued for the clinical significance of depressed mood (McCain & Zeller, 1996).

Other groups of investigators suggested that the chronic stress, psychological distress, and depression observed in HIV+ subjects were not related to decline of

immune parameters and disease progression. In a cohort of 1,339 HIV+ men, Lyketsos et al. (1993) found no differences between depressed and non-depressed subjects in the rate of CD4+ decline or other indicators of disease progression over a 5-year period. However, depressed subjects had lower CD4+ counts and reported more symptoms at baseline. A cross-sectional study of 124 HIV+ men, with repeated measures at 6 months, found no concurrent or predictive relationships between CD4+ and CD8+ immune measures and depression, anxiety, psychological distress, number of life stressors, bereavement, or social support (Rabkin et al., 1991). Finally, Kessler, Foster, Joseph, Ostrow et al. (1991) concluded that serious stressor events were not related to HIV symptom onset, defined as a 25% decline in CD4+ percentage over a 6-month period.

While cumulative data are limited and effect sizes are modest, there is general support for relationships between psychological distress, stress/coping patterns, clinical symptoms, and immune measures in the HIV+ population (McCain & Zeller, 1996). Psychological distress may be a common denominator for PNI-related immunosuppression (Kiecolt-Glaser & Glaser, 1992) and thus is a key outcome variable in studies of stress. Possible reasons for some of the inconsistent findings in the HIV+ population may be related to heterogeneity of subjects on disease stage, health behaviors, gender, and differences in immunological measures (Kiecolt-Glaser & Glaser, 1995; McCain & Zeller, 1996; Zeller, McCain, McCann et al., 1996).

Physiological and Behavioral Mechanisms Associated with Stress and Immunity in HIV

The hallmark of HIV disease is progressive loss of CD4+ T-lymphocytes; thus, stress-induced HPA axis activation might be an important co-factor of HIV disease progression (Gorman et al., 1991). Patients with HIV infection are prone to chronic activation of the HPA axis, resulting in elevated serum cortisol levels, compromised cellular immune responsiveness, and the promotion of viral replication (Azar & Melby, 1993; Biglino et al., 1995; Kirschbaum et al., 1995; Norbiato, Bevilacqua, Vago, Taddei, & Clerici, 1997). Stress leads to an increase in latent herpes virus, and, because HIV can latently affect lymphocytes, parallels between psychosocial mediation of latent herpes virus infection and HIV have been proposed (Kiecolt-Glaser & Glaser, 1995).

It is plausible that elevated levels of cortisol associated with chronic stress may accelerate the course of HIV, either by suppressing the function of immune cells that carry out antiviral activities (Migliorati et al., 1994), by encouraging a predominate type 2 as opposed to type 1 cytokine response pattern leading to a decrease in cellular immune function (Norbiato et al., 1997), or by enhancing HIV replication in infected cells by binding to the genome (Kolesnitchenko & Snart, 1992). In addition to depression of T-lymphocyte number and function, in vitro evidence suggesting that glucocorticoids enhance viral replication (Markham, Salahuddin, Veren et al., 1986) has been reported. Thus, the over secretion of cortisol characteristic of many HIV infected individuals may be critically involved with regulation of immune function and poorer prognosis. A small subset of HIV+ subjects develop resistance to the immunosuppressive effects of cortisol leading to recovery of the cellular immune

response; however, studies of cortisol resistance have been conducted primarily on patients with AIDS, and cortisol resistance has not been observed to change the course of the disease (Norbiato et al., 1997).

Cortisol and other neuroendocrine indicators of chronic stress are frequently not used in PNI research in the HIV population because of issues of measurement validity and the need to control for circadian periodicity (McCain & Zeller, 1996). One study of 113 HIV+ and 77 HIV- subjects found small but significant correlations between cortisol level and medical status ($r = .20$), level of depression ($r = .25$), symptoms ($r = .19$), and level of anxiety ($r = .23$); however, cortisol was not related to CD4+ or CD8+ T-lymphocyte level (Gorman et al., 1991). The authors concluded that, although HPA axis activation may be associated with stress in HIV-infected subjects, it does not seem to be associated with further loss of CD4+ cells. In this sample, degree of HPA axis activation as reflected in urinary free cortisol was minimal; therefore, cortisol levels may not have been of sufficient magnitude to impact immune function.

A correlational study of neuroendocrine patterns during the week of serostatus notification in 25 HIV+ and 46 HIV- men (Antoni, Schneiderman et al., 1991) reported an inverse correlation between cortisol and concurrent measures of psychological distress ($r = -.67$). On the other hand, cortisol levels were positively correlated with increased T-lymphocyte proliferation response ($r = .56$). This is contrary to the PNI-predicted relationships of increased distress being positively correlated with cortisol levels, and elevated cortisol in turn positively correlated with decreased T-lymphocyte proliferation. The one-time salivary cortisol samples collected for this study had

inherent variability, and this may help to account for the findings. The measurement and interpretation of neuroendocrine parameters, particularly for studies of naturalistic and chronic stress, remain problematic yet important for progress in HIV research (McCain & Zeller, 1996).

Behavioral changes associated with HIV, such as eating patterns, sleep, or drug use, may also contribute to disease progression (Kemeny, 1994b; Kennedy, Glaser, & Kiecolt-Glaser, 1990), as suggested in the Biobehavioral Model adapted for this study. A seminal review of 36 PNI studies in HIV disease (McCain & Zeller, 1996) documented the current need for design and statistical evaluation strategies for such variables as neuropsychological functioning, age, nutritional status, sleep patterns, physical activity, use of alcohol or psychoactive drugs, and menstrual phase. Compliance with immuno-regulatory medications was also of particular importance (McCain & Zeller, 1996; Kiecolt-Glaser & Glaser, 1988; Zeller McCain, McCann et al., 1996).

Relaxation as Stress Management

A recent 20-year review of relaxation literature documents that relaxation has been used as an effective stress management tool to reduce psychological distress, improve quality of life, modify depression, and treat a variety of physical symptoms (Lehrer, Carr, Sargunraj, & Woolfolk, 1994). In addition to demonstrated benefits in modifying psychological distress, evidence suggests that relaxation and imagery may contribute to improved quality of social relationships and to enhanced cellular immune

function and therefore may be important in mediating the immune response to stress (Antoni et al., 1990; Antoni, Baggett et al., 1991; Gruber et al., 1993; Hall, & O'Grady, 1991; Halley, 1991; Kiecolt-Glaser & Glaser, 1995; McCain, Zeller, Cella, Urbanski, & Novak, 1996; McEwen, 1998; Rider et al., 1990; Solomon et al., 1991; Zachariae et al., 1994).

The psychological and immunological effects of relaxation have been tested in acute laboratory stress conditions. A study of 24 healthy adult subjects randomly assigned to experimental or no-treatment control groups showed that, compared to controls, subjects trained in relaxation improved on measures of mental state and showed a decreased T-lymphocyte and interleukin-1 response after exposure to the acute stressor (Johnson, Walker, Heys, & Whiting, 1996). In another laboratory controlled study, 65 adult college students were classified as high or low in hypnotizability using the Stanford Hypnotic Susceptibility Scale and randomly assigned to a relaxation-imagery (hypnosis), Restricted Environmental Stimulation Therapy (REST), or control condition (Ruzyla-Smith, Barbasz, Barbasz, & Warner, 1995). Findings showed significantly greater CD4+ T-lymphocyte counts for those highly hypnotizable subjects in the relaxation/imagery condition compared to other groups. Relaxation also has been shown to reduce delayed-type hypersensitivity (DTH) reactions to an experimental allergen (Zachariae, Jorgensen, Christensen, & Bjerring, 1997).

Studies of healthy adults in naturalistic settings suggest that relaxation may modify the immune response to an acute stressor and compliance with relaxation

practice schedules may importantly contribute to immune outcomes. In a study of 45 geriatric subjects, Kiecolt-Glaser et al. (1985) found that the daily practice of relaxation with guided imagery for six weeks resulted in a reduction in psychological distress, enhanced sleep quality, an increase in NKCC, and a decrease in antibody response to Herpes Simplex Virus (HSV). However, these benefits did not persist after practice was discontinued, suggesting that regular relaxation practice may be necessary to maintain benefits. Among medical students undergoing examination stress, Kiecolt-Glaser et al. (1986) showed that, whereas students who were not trained in relaxation exhibited significantly increased distress and significant declines in percent of CD4+ cells, CD4+/CD8+ cell ratio, and NKCC, those students who were trained and practiced relaxation exhibited no such negative consequences. Further, Kiecolt-Glaser et al. (1986) found that practice frequency was the best predictor of the CD4+ response to examination stress. Finally, McGrady et al. (1991) used a 4-week pretest-posttest design to study 31 medical students assigned to a relaxation or control condition. The treatment group ($n = 14$) received autogenic relaxation training with biofeedback. Results indicated the relaxation group had a positive outcome with significantly increased blastogenic response to an allergen (PHA) and a decreased white blood cell (neutrophil) response.

Additionally, use of relaxation and imagery to modify the cellular immune response to stress has been found in studies of cancer patients (Anderson et al., 1994; Burish & Tope, 1992; Edwards, 1990; Kiecolt-Glaser & Glaser, 1995; Lekander, Furst, Rotestein, Hursti, & Fredrikson, 1997a, 1997b; Maier et al., 1994; Su, Tan, &

Zheng, 1997). A review of Vanderbilt University's 10-year research program designed to treat the ongoing stress-related side effects of chemotherapy suggested that relaxation and guided imagery reliably reduced various measures of treatment distress more than any other single behavioral intervention. Additionally, relaxation interventions were most effective when introduced early in the treatment process (Burish & Tope, 1992).

Gruber et al. (1993) provided a 9-week relaxation with biofeedback instruction to 13 breast cancer survivors. Subjects were divided into an experimental and wait-list control group with repeated measures and follow-up for 18 months. They found that relaxation significantly improved survivors' cellular immune response as measured by blastogenic response to Con A, NKCC, and increased total T-lymphocytes numbers. B-cell mediated (humoral) immunity was not affected. Three months were needed to detect significant immunological change. Significant reductions in anxiety, along with enhanced joy, fighting spirit, and ego strength were also found. Additionally, quality of social support improved, despite a decrease in the number of people providing social support. Post hoc analysis showed the improvement in overall social support highly correlated with amount of relaxation practice.

One prospective longitudinal investigation evaluated the immediate and longer-term effects of a 6-week structured group intervention that included relaxation for post-surgical patients with stage I or II malignant melanoma (Fawzy et al., 1990a, 1990b). The experimental ($n = 38$) and control ($n = 28$) subjects were measured at baseline, immediately after the 6-week intervention, and again after 6 and 12 months. Short-term differences included increased vigor, greater use of active coping, and significant

changes in NK number. After 6 months, group differences were more notable. Experimental subjects showed significantly lower depression, fatigue, confusion, and total mood disturbance as measured on the Profile of Mood States and exhibited more active behavioral and cognitive coping as measured on the Dealing with Illness-Coping Inventory. Additionally, experimental subjects showed significant increases in percent of NK cells and an increase in NK cell cytotoxicity, results that were maintained after 12 months. A 6-year follow-up showed a trend toward greater recurrence and a statistically significant higher mortality rate in control patients, even after adjusting for size of the initial malignant melanoma lesion (Fawzy & Fawzy, 1994; Fawzy et al., 1990b).

Physiological and Behavioral Mechanisms Associated with Relaxation

Relaxation has been hypothesized to influence the same neuroendocrine mechanisms activated during stress, namely the HPA axis and the SNS (Benson, 1975, 1982, 1983; Gruber et al., 1993; Sakakibara, Takeuchi, & Hayano, 1994). Using electrocardiograms and pneumograms to record heart rate variability in a group of 16 college students, Sakakibara et al. (1994) showed that autogenic relaxation training was associated with an increase in parasympathetic tone. They suggested enhanced cardiac parasympathetic tone may explain an important mechanism underlying the beneficial effect of the relaxation response.

Three clinical studies investigated the possible beneficial effects of relaxation therapy on HPA axis activation as assessed by cortisol levels. Gruber et al. (1993)

noted a significant decrease in plasma cortisol in breast cancer survivors after 6 months of relaxation training; however, this finding was not replicated when the wait-list control group underwent training. Manyande et al. (1995) found that relaxation and guided imagery provided to a group of 26 experimental surgical patients significantly lowered plasma cortisol immediately before induction of anesthesia and post-operatively, compared to 25 matched control subjects. The authors suggested that this study supported the effectiveness of imagery as an active coping strategy in response to acute stress. In contrast, McGrady et al. (1991) reported no change in cortisol levels among medical students participating in a 4-week relaxation and biofeedback program. The authors suggested that more time may have been needed to obtain a response.

HIV, Relaxation, and Disease Progression

Research exploring possible benefits of relaxation and imagery in HIV patients is sparse; however, results are promising (Kiecolt-Glaser & Glaser, 1992; McCain & Zeller, 1996). Studies to date involve stress management approaches using cognitive-behavioral techniques or aerobic exercise training (McCain & Zeller, 1996). An early study by Coates, McKusick, Kuno, and Stites (1989) randomized 64 HIV+ men into experimental or wait-list control groups. The treatment group met for eight 2-hour sessions and one all-day retreat (8-week program) to learn systematic relaxation, health behavior change, and stress management skills. Subjects reported significantly fewer sexual partners; however, no group differences were found for number of CD4+ T-lymphocytes, CD4+/CD8+ ratio, NK cell cytotoxicity, or lymphocyte proliferative

response. Baseline CD4+ counts, antiviral medication use, and stage of illness were not well described, making immunologic findings for this study difficult to interpret (McCain & Zeller, 1996).

An intervention study by Auerbach, Oleson, and Solomon (1992) randomized 20 symptomatic HIV+ men to a wait-list control or an 8-week training program in thermal biofeedback and guided imagery. Intervention was associated with a decline in self-reported symptoms and increases in vigor as measured by the Profile of Mood States. No significant differences were found between groups in CD4+ cell numbers or other measures of psychological distress; however, CD4+ data were obtained from independent physicians' records, and the timing of intervention to CD4+ data was not described.

The University of Miami, Center for the Biopsychosocial Study of AIDS, has conducted studies for the HIV population using aerobic exercise and cognitive behavioral stress management as intervention strategies. Five weeks before notification of their HIV serostatus, 47 healthy asymptomatic men were randomly assigned to a stress management or assessment-only control condition (Antoni, Baggett et al., 1991; Antoni, Schneiderman et al., 1991). The cognitive-behavioral stress management program incorporated relaxation. Subjects were assessed after the training period and 72 hours before notification of serostatus, with one additional measurement 7 days after notification. Seropositive intervention subjects showed significant increases in CD4+ and NK cell counts and a decrease in antibody titers to latent herpes virus type 6 (HHV-6) (Esterling et al., 1992) and had much lower depression scores on the Beck

Depression Inventory compared to controls. There were no significant differences between groups in lymphocyte proliferative response or NK cell cytotoxicity. Parallel results were found for 60 HIV+ men who participated in an exercise intervention (Esterling et al., 1992; LaPerriere et al., 1990). Similar to the findings of Kiecolt-Glaser et al. (1985, 1986), frequency of relaxation practice correlated significantly with lower depression scores, higher CD4+ counts, and higher NK cell counts.

Eller (1995) compared two cognitive-behavioral techniques among 45 people at various stages of HIV illness using a pretest-posttest design. Subjects were randomized into one of three conditions—a progressive muscle relaxation only group, a guided imagery only group, and a control group. Following the 6-week audio taped intervention, the relaxation group had significantly less depression as measured by the Center for Epidemiological Studies-Depression Scale and significantly higher post-intervention CD4+ lymphocyte counts than did the control group. No differences were found between these two groups in number of NK cells. Subjects who participated in the guided imagery only group had significantly less depression and fatigue (Sickness Impact Profile) compared to controls; however, immunological measures were not significantly different. Eller suggested that stress resulting from the virus-specific guided imagery might account for the absence of immune modulation in the imagery only group.

In another recent intervention study, McCain et al. (1996) used a pretest-posttest nonrandomized design to compare the effectiveness of a 6-week stress management program with standard outpatient care for men with HIV (30 for the intervention group

and 15 for comparison). The program consisted of relaxation training (progressive muscle relaxation, yogaform stretching with integrative breathing) and mental imagery. At 6 weeks, no differences were found between groups. However, among the men trained in relaxation and imagery, the Emotional Well-being Subscale (Functional Assessment of HIV Infection) was found to be significantly higher following intervention. Additionally, frequency of practice was found to be significantly associated with increased positive impact stress, higher quality of life, less avoidant thinking, more frequent use of problem-focused coping, and less uncertainty, suggesting that training may have buffered psychological distress. At 6 months, Emotional Well-being scores were not sustained for intervention subjects; however, significant differences in intrusive thinking (Impact of Event Scale) were observed. Analysis of immunological data showed that the intervention group had no change from baseline CD4+ counts, whereas comparison subjects exhibited an average decline of 22 cells/ μ l. CD4+ T-lymphocyte data were collected on a subsample of subjects, and insufficient power may have contributed to the inability to achieve statistically significant differences between groups. The authors suggested that this brief intervention had a positive short-term impact on emotional well-being (a quality of life measure) and a long-term impact on overall psychological distress (McCain et al., 1996).

Finally, the efficacy of relaxation was tested in a sample of HIV+ men in the early stages after infection by comparing three groups: relaxation (progressive muscle and autogenic), supportive psychotherapy, and a no treatment control group (Fukunishi et al., 1997). No group differences in total mood disturbance (measured by the Profile

of Mood State) were found among the three groups. However, subjects participating in the relaxation training were significantly lower post-intervention on subscales for anxiety, fatigue, depression, and confusion. These results suggest that a combination of progressive muscle relaxation and autogenic training is a useful method to reduce psychological distress in HIV patients without AIDS.

Summary

In addition to the growing body of research supporting the benefits of relaxation and imagery in the cancer population (Anderson et al., 1994; Fawzy & Fawzy, 1994; Gruber et al., 1993; Herbert & Cohen, 1993a; Lekander et al., 1997a, 1997b; Maier et al., 1994; McCain & Zeller, 1996; Sims, 1987; Spiegel & Moore, 1997; Trusburg, van Knippenberg, & Rijkman, 1992), HIV+ intervention studies provide evidence suggesting that relaxation may reduce psychological distress, enhance quality of life, and reduce stress-related immunosuppression in people with HIV and underscore the need for further investigation. Use of a PNI framework for ongoing investigations is critical to understanding the relationship between quality of life factors, including psychological distress and symptomatology, and disease progression (Kiecolt-Glaser & Glaser, 1992; McCain & Zeller, 1996). Relaxation training is increasingly recognized as an important component of any comprehensive stress management program and may be particularly important for immunosuppressed populations (Fawzy & Fawzy, 1994; Halley, 1991; Kiecolt-Glaser & Glaser, 1992; McCain & Smith, 1994; Rokicki et al., 1997; Rider et al., 1990). The technique portends to reduce costs associated with

chronic illness and enhance quality of life among those afflicted with HIV (Baum et al., 1995; Wallace, 1997). HIV infection is a “devastating, chronic, debilitating disease,” and prospective, longitudinal studies to test the effectiveness of interventions that enhance quality of life and promote immunocompetence are a clear priority for nursing research (McCain & Zeller, 1996).

CHAPTER 3

METHODOLOGY

Design

This study examined the effect of a 12-week relaxation protocol on (a) psychological distress, (b) quality of life, (c) health behavior, (d) salivary cortisol, (e) CD4+/CD8+ ratio, and (f) viral load in HIV-infected adults. The study used an experimental wait-list control group design. Subjects randomized into the experimental group began relaxation training immediately after enrollment (week 1), and subjects randomized to the control group were eligible to begin relaxation training after their 12-week waiting period. Outcome data were collected at the beginning of training (week 2) and repeated at weeks 6, 10, and 14.

Sample

The target population included HIV+ subjects who expressed interest in using relaxation as a method of individual stress management. A convenience sample of 40 volunteer subjects was obtained through advertising in The Ohio State University AIDS Clinical Trials Unit (ACTU) cohort (OSU Protocol #87HO305), the Columbus and Dayton AIDS Task Force, an ACTU-affiliated women's support group, and other community agencies and hospitals serving the HIV+ population. The sample included

both males and females and a racial composition reflective of minority representation in the above-mentioned agencies. All subjects were randomized into the experimental or wait-list control group condition based on a 2:1 ratio, experimental to control, by using a 3x6 permuted block technique (Rudy, Vaska, Daly, Harp, & Shiao, 1993). Specifically, a table of random numbers was used to develop a set of cards that randomized the experimental and control condition in randomly assigned blocks of 3 and 6. Vertical randomization was used to determine the permuted blocks with even numbers assigned as a block of 3 and odd numbers assigned as a block of 6. Cards were then assigned as experimental or control using even numbers as the control condition and odd numbers as the experimental condition. The cards were sealed in an envelope and labeled from 1 to 60. Subjects were later assigned to either the experimental or control condition by receiving cards in order of their scheduled enrollment.

Inclusion and Exclusion Criteria. Both male and female subjects were included if they met the following criteria: (a) between the ages of 18-50; (b) documentation of HIV infection; (c) subject knowledge of the diagnosis for 4 months; (d) stable viral load (less than a 2-log change) within six months; (e) no concurrent participation in a meditation or relaxation program; (f) able to schedule 6 General Clinical Research Center (GCRC) visits; and (g) willingness to practice regularly. Subjects were excluded based on: (a) greater than two infectious illnesses requiring hospitalization in the past 12 months; (b) starting or changing anti-retroviral or anti-depressant medication within 8 weeks prior to entry; (c) current drug abuse including alcohol; and (e) cognitive impairment suggesting hallucinations or dementia. Experimental subjects

received an incentive fee of \$100 for participation. Control subjects received \$100 if they met the data collection requirements and an additional \$100 after completing the 12-week program.

Sample Size. A sample of 30 subjects was deemed necessary for this study based on review of literature and power analysis using standard statistical power software (Borenstein & Cohen, 1998). The required sample size was calculated from the means and standard deviations of MOS-HIV scores previously reported for HIV+ subjects (Wu et al., 1997). Higher scores on this instrument reflect higher quality of life. A MOS-HIV baseline mean of 37.7 and standard deviation of 22.2 was projected for this sample with one standard deviation increase (mean of 59.9) projected for experimental subjects post-intervention. The projected sample size of 30 subjects assumed a large effect size with statistical power = 0.80, at alpha = .05 (1-tail test of significance). The sample size was then compared to reported relaxation therapy studies with significant outcomes in HIV, oncology, and other patient populations. In a sample of experimental treatment ($n = 7$) and delayed treatment control group ($n = 6$) breast cancer subjects, Gruber et al. (1993) reported that relaxation and guided imagery led to significant between-group differences in salivary cortisol over an 18-month timeframe. Other investigators have documented a significant between-group effect on cortisol level post-operatively after short-term use of relaxation and imagery for a randomized post-surgical sample of 26 experimental and 25 control subjects (Manyande et al., 1995). Thus, the projected sample size of 20 experimental and 10 control subjects appeared reasonable, based on both statistical considerations and the reported research.

This sample estimate was increased to 40 to allow for attrition over the 12-week protocol.

Human Subjects Protection. The study protocol was approved by the OSU Biomedical Review Committee (96H0451). Confidentiality of records was maintained according to GCRC policy by use of subject ID numbers on all questionnaires and laboratory report forms. The GCRC also provided a locked file cabinet, a room for private interviews, and storage of all subject data and records. Risks for participating in the study were deemed minimal.

Setting

Subject recruitment was conducted in collaboration with The Ohio State University Aids Clinical Trial Unit (ACTU). The Unit also provided access to medical records for the medical screening and viral load data required to determine subject eligibility. The ACTU is one of 35 adult units funded by the National Institutes of Health to conduct trials of experimental therapies for HIV-1 infection.

Relaxation training and data collection were conducted at The Ohio State University Hospitals General Clinical Research Unit (GCRC), a clinical research setting funded by the National Institutes of Health. The GCRC provided an environment conducive to relaxation training and privacy for all training sessions. In addition, Unit personnel assisted with scheduling, accurate storage, and labeling of salivary cortisol samples, venipuncture for immune and viral load data, and assistance with data

management procedures. The GCRC also provided funding for collection and analysis of salivary cortisol, CD4+/CD8+ and viral load data.

Independent Variable

The independent variable of interest was a 12-week program of relaxation and guided imagery (active coping protocol). Details of the training are provided later in this chapter. Subjects received training in focused breathing, autogenic relaxation methods, centering, and progressive relaxation of major muscle groups (Benson, 1975; Burish & Lyles, 1981; Dossey, Keegan, Guzzetta, & Kolkmeier, 1988; Lehrer et al., 1994). In addition, subjects learned standard imagery techniques (Achterberg, Dossey, & Kolkmeier, 1994; Bauer & Craighead, 1979; Brown, 1983; Christman & Kirkoff, 1985; Horowitz, 1970; Vines, 1988) designed to support muscle, visceral, and emotional relaxation. The standard imagery exercises focused on one or more of the following categories: (a) an image of the problem or stressor of greatest concern, (b) an image of internal healing resources, and (c) an image of external healing resources. Standard imagery techniques were adapted as necessary for the specific issues identified by each subject as causing the most stress in his or her current life circumstance. For example, a subject complaining of peripheral neuropathy could learn to adapt the general relaxation technique for pain management, while a subject complaining of generalized anxiety could learn to focus on general physical tension and anxiety. Thus, subjects were taught to use general relaxation and associated imagery exercises as an active coping method for their specific stressor(s). Subjects agreed prior to enrollment

to practice relaxation methods at least 15 minutes a day, 5 times a week, and to monitor their progress on weekly practice logs.

Ability to achieve a relaxation response was operationally defined by both objective and subjective criteria (McGrady, 1994). In particular, any elevation in peripheral finger temperature (Bio-Medical Instruments Stress Computer recorder) constituted the objective measure of relaxation, and a self-rating of experienced relaxation constituted the subjective measure of relaxation. The training program was pilot tested for two subjects in the GCRC. Both subjects identified stress as a major reason for interest in the program and entered training with intent to incorporate relaxation into their lifestyles as a routine method of stress management. Pilot data suggested that subjects were both willing and able to achieve agreed-upon practice requirements throughout the 12-week program.

Dependent Variables

The dependent variables defined for this study included Psychological Distress (Profile of Mood States), Quality of Life (Medical Outcomes Study HIV), HPA axis (Salivary Cortisol), Disease State Marker (CD4+/CD8+ ratio and Viral Load), and Health Behavior (Health Behavior checklist). Data on level of social support and number of HIV-related symptoms were also collected to help explain and validate the dependent variables of interest. Table 1 provides a summary of hypotheses, dependent variables, and measures used for this study. The instruments used for data collection are provided in Appendix A.

Hypotheses	Dependent Variables	Measures
Hypothesis 1	Psychological Distress	POMS (total and 6 subscales)
Hypothesis 2	Quality of Life	MOS-HIV (total and 11 subscales) Symptom Checklist
Hypothesis 3	HPA Axis	AM/PM Salivary Cortisol
Hypothesis 4	Disease State Marker	CD4+/CD8+ Ratio Viral Load
Hypothesis 5	Health Behaviors	Health Behavior checklist

Table 1. Summary of Hypotheses, Dependent Variables, and Measures

Profile of Mood States (POMS).

For this study, perceived psychological distress was assessed by patient report using the POMS. The POMS (McNair, Lorr, & Droppleman, 1992) is a 65-item paper and pencil self-administered instrument comprised of 6 subscales: Tension/Anxiety, Depression/Defection, Anger/Hostility, Fatigue/Inertia, Confusion/Bewilderment, and Vigor/Activity. The inventory has been standardized for both psychiatric and nonpsychiatric samples and is frequently used as a sensitive measure of mood changes in short-term (4- to 12-week) interventions, including relaxation, meditation, and brief psychotherapy (McNair et al., 1992). Several studies report evidence of the discriminate and construct validity of the POMS in that subscale factors are sensitive to change associated with brief interventions and measures do not change simply as a function of repeated testing during treatment (Haskell, Pugatch, & McNair, 1969; Lorr, McNair, & Weinstein, 1964; McNair et al., 1992). The total mood score on the POMS correlates significantly with scores on the Hamilton Depression Inventory ($r = .78$; $p < .001$), and the depression subscale has been shown to positively correlate with the

Beck Depression Inventory ($r = .80$; $p < .0001$) (Malouff, Schutte, & Ramerth, 1985; Seluka, 1997). In addition, the POMS is able to discriminate depressed subjects from nondepressed matched controls, and total POMS scores have been shown to correlate with baseline cortisol levels in depressed subjects (Seluka, 1997). The instrument has been used as a sensitive measure of psychological distress in a number of recent studies with HIV and cancer populations (Fawzy et al., 1990a; LaPerriere et al., 1990; McCain et al., 1996; Mulder et al., 1994). LaPerriere et al. (1990) used the POMS to explore possible benefits of exercise in subjects undergoing HIV testing. Pretest to posttest differences were detected between exercisers versus non-exercisers in response to the acute stressor of seropositive diagnosis on the anxiety and depression subscales. Additionally, the POMS was used by Antoni, Baggett et al. (1991) in a cognitive behavioral stress study to assess distress at notification of seropositive status in HIV subjects. They found that the increase in mean depression scores for seronegative controls was more than double the increase for seropositive controls involved in the stress management intervention. The instrument is scaled so that lower scores were indicative of improved mood state and higher scores indicated more mood distress.

Medical Outcomes Study HIV (MOS-HIV).

The MOS-HIV short-form health survey assesses quality of life outcomes in the following areas: overall evaluation of health, functional status, well being, and change in health. Psychometric analysis of responses by 520 HIV-infected people with sociodemographic characteristics similar to those of the general population support

reliability and validity of the instrument as a quality of life measure for this population (Wachtel et al., 1992). Scores on the MOS-HIV correlate significantly with those on the Quality of Well-Being Scale ($r = .67$; $p = .01$), another instrument frequently used to assess quality of life in HIV subjects (Copfer et al., 1996). The MOS-HIV requires less than 5 minutes to complete and appears to be sensitive in detecting treatment differences in clinical trials (Bozzette, Hays, Berry, Kanouse, & Wu, 1995; Calantino, 1997). Higher scores on the MOS-HIV reflect higher quality of life.

Salivary Cortisol, T-Lymphocyte Count and Ratio, and Viral Load.

Salivary cortisol served as an overall marker of general stress. Salivary cortisol is an inexpensive, easily collected, noninvasive method to measure HPA axis activation and provides a valid and reliable measure of biologically active plasma cortisol when collected according to the standardized procedure (Ellison, 1988; Vining & McGinley, 1987). Because cortisol levels in saliva are not affected by corticosteroid-binding globulin present in serum proteins, salivary cortisol levels are believed to more sensitively reflect adrenal status than is serum cortisol (Kirschbaum & Hellhammer, 1989; Rolih & Ober, 1995; Vining, McGinley, Maksvytis, & Ho, 1983).

The disease state markers of interest included immune system data, specifically CD4+ T-lymphocyte count, CD8+ T-lymphocyte count, CD4+/CD8+ ratio, and viral load. The immune system outcome measures were selected for their potential responsiveness to stress management intervention (Antoni, 1991; LaPerriere et al., 1994; Zeller, McCain, & Swanson, 1996). Viral load was included as a disease state

marker in this study with intervention effects on viral load hypothesized. Ability to quantify HIV viral load is a recent advancement (Caliendo, 1995; Zeller, McCain, & Swanson, 1996), and relaxation studies in the HIV population have not previously included this disease marker as a dependent variable. All biological measures mentioned above were selected based on the Biobehavioral Model (Anderson et al., 1994) used as a framework for this study.

Health Behavior.

The Health Behavior Checklist used for this study was adapted from literature relative to behavior known to influence validity of salivary cortisol and other neuroendocrine data (Kiecolt-Glaser & Glaser, 1988; Zeller, McCain, McCann et al., 1996) and from data collected in a study of the effects of aerobic exercise in HIV subjects (Smith, Neidig, MacVicar, Nickel, & Salsberry, 1994). The instrument assessed change in several health behaviors over the previous 4-week period including: nutrition; general level of physical activity; the amount, frequency, and type of regular aerobic exercise; alcohol consumption; tobacco use; and quality of sleep. The GCRC nutritional assessment tool was added to the checklist to provide additional data relative to nutritional status. This form, developed by the research dietitian in the GCRC, is routinely used in GCRC study protocols.

Related Variables and Measures

Social Support Questionnaire (SSQ6).

Social factors, particularly level of social support, are well known to have a major influence on the neuroendocrine response to stress (Cohen et al., 1992; Kamarck, Annunziato, & Amateau, 1995; Malarkey et al., 1994; Unicho et al., 1992). This variable was measured primarily to determine baseline differences between groups and as a reference for interpretation of outcomes. The SSQ6 is a 6-item social support measure derived from the original widely used 27-item Social Support Questionnaire (SSQ). The SSQ6 is easily administered and has been shown to provide a valid measure of social support; test-retest and internal reliability scores are psychometrically sound. Additionally, SSQ6 scores have been shown to correlate with scores on the SSQ (longer version) and to a variety of personality and social competence variables associated with social support (Sarason, Sarason, Shearin, & Pierce, 1987). The instrument measures (a) the number of people providing social support under conditions of stress, tension, and depression, and (b) the perceived quality of that support, so that higher scores indicate higher number and perceived quality. ACTU cohort studies routinely use the SSQ6 as an index of social support for HIV patients.

Symptom Checklist (Sx Checklist).

An HIV symptom-related checklist used to document health-related symptoms in ACTU cohort studies was used to assess 20 symptoms-such as fatigue, nausea, vomiting, neuropathy, and pain-which are commonly associated with medication and

disease factors in the HIV population. The checklist was adapted for this study to determine whether or not experimental subjects began use of relaxation for symptom management. Data from this checklist was used to validate symptom-related quality of life measures obtained on the MOS-HIV.

Confounding Variables.

Data on the following potentially confounding variables was also collected during each GCRC visit: (a) protocol or drug changes; (b) significant life stress events such as economic status or loss of significant other; and (c) infectious or neuroendocrine disease (Norbiato et al., 1997).

Enrollment, Training, and Data Collection Procedure

Enrollment. The enrollment interview was designated as Study Week 1. ACTU staff members referred patients who expressed interest to the study, and the investigator made an initial telephone contact. Next, CD4+, viral load, and medical history data were reviewed to ensure the subject met entry criteria. Once eligibility was established, subjects were scheduled for an enrollment interview in the GCRC. During the enrollment interview, the medical history was reviewed and updated, a thorough explanation of the study was provided to ensure subjects understood the 12-week training commitment required for participation, and a practice contract was agreed upon between the principal investigator and each subject, with a minimal level set at 15 minutes per day, 5 days a week. An incentive fee of \$100 was provided to each subject

who met the agreed-upon practice requirement, and this information was reviewed with each subject. Informed consent to participate was documented by a signed consent form (IRB #96H0351). Subjects were then randomized to the experimental or control condition, a written training schedule was developed, and the first training/data collection was scheduled with the GCRC unit secretary. All subsequent visits were scheduled for the same day each week when possible. Subjects were provided with verbal and written instructions for collection of salivary cortisol. Forms used for enrollment are provided in Appendix B. The schedule for enrollment, training, and data collection is shown in Table 2.

	Study Weeks														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
TRAINING	Enroll		cv	cv	hv	ph	cv	ph	cv	ph	cv	ph	ph	ph	cv
Practice Record				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
MEASURES															
CD4+/CD8+	✓														✓
Viral Load	✓														✓
MOS/HIV			✓				✓				✓				✓
POMS			✓				✓				✓				✓
Salivary Cortisol			✓				✓				✓				✓
Health Behavior			✓				✓				✓				✓
SSQ6			✓				✓				✓				✓
Sx Checklist			✓				✓				✓				✓

cv = clinic visit; ph = telephone; hv = home visit.

Table 2. Schedule of Training and Repeated Measures

Training. The time from enrollment to initial training was generally 1 to 3 weeks, depending on room availability and subject preferences. The first scheduled training and data collection date was designated as Study Week 2 (baseline). Relaxation instruction was conducted in 2-hour time blocks in the GCRC beginning study week 2, with additional instruction on weeks 3, 4, 6, 8, 10, and 14 (12 weeks of training).

Training in the home setting was conducted during week 4 for those subjects who elected a home visit. The investigator contacted subjects during off weeks (weeks 5, 7, 9, 11, 12, and 13) by telephone for problem-solving, education, and practice support.

At the first training session, subjects received a notebook for storage of training material, verbal and written instruction on use of finger temperature biofeedback equipment, and an explanation of what would be covered during the training session. Subjects were guided through the initial relaxation exercise, and an individualized audio tape recording was made to support daily practice. At end of the first session, subjects were taught how to complete the daily practice log, and methods to support the minimum 15-minute, 5 days per week, practice requirement were reviewed.

Each subsequent training session followed a standard procedure of Assessment, Intervention, and Evaluation/Integration. Practice logs and any practice difficulties were reviewed, along with an assessment of any new life stressors. This information was used to adapt the specific exercise, as needed, for the individual subject. For example, if a subject was having difficulty with focused breathing, greater emphasis was given to this specific technique during the session. Thus, while all subjects received the same overall training protocol, the speed at which they were able to use and integrate the techniques varied by individual. At the end of the training session, subjects discussed how to use the experience during practice. Over the course of the 12-week program, subjects received a copy of all training exercises, along with articles explaining the uses of various relaxation and imagery techniques. An overview of the training protocol and imagery exercises is provided Appendix C.

Data Collection. A weekly practice log was developed for this study. Data included time and frequency of practice, skin temperature (biofeedback) response, and a subjective rating of relaxation. For subjects in the experimental condition, practice logs were collected at each training point, and questionnaire and salivary cortisol data were collected every 4 weeks (week 2 to entry, 6, 10, and 14 to exit) immediately prior to scheduled GCRC training sessions. Control subjects were scheduled for data collection (cortisol and questionnaires) at weeks 2, 6, 10, and 14. On week 14, control subjects began their 12 weeks of relaxation training. Data collection for control subjects after entry to the experimental protocol was conducted from weeks 14 to 26, according to the schedule outlined above for experimental subjects.

Salivary cortisol collection was standardized at designated time points to control for diurnal variation (Vining & McGinley, 1987). Two samples of saliva (AM and PM) were obtained for each repeated measure. Subjects were provided with labeled salivettes and instructed to obtain samples between 5:00 to 7:00 PM the evening before and between 7:00 to 9:00 AM the morning of scheduled training in the GCRC. All subjects received written instructions on use of the salivette and the procedures required for a valid cortisol sample, including cleansing of the mouth and avoidance of caffeine, nicotine, or other food intake 30 minutes prior to sample collection (Ellison, 1988). All samples were refrigerated in the GCRC and processed for storage by GCRC laboratory personnel within 4 to 6 hours after being received. The salivettes were centrifuged, and the saliva obtained was captured for long-term storage. Samples were stored in the

GCRC research laboratory at -80°C for batch assay at the end of the study (Ellison, 1988; Vining & McGinley, 1987).

CD4+, CD8+, and viral load data were collected by GCRC staff at week 2 and at week 14. Control subjects who completed the relaxation protocol had blood drawn at week 26. Any subject who had immune and viral load data drawn for other ACTU protocols within 3 weeks prior to study entry or exit could request that those data be used, and these data were subsequently obtained from the subjects' medical records. CD4+ and CD8+ levels were assessed using standard flow-cytometric techniques on freshly drawn EDTA-chelated whole venous blood specimens. To control for possible interlaboratory variation, CD4+ and CD8+ immunophenotyping and HIV-viral load assays collected in the GCRC were performed in the OSU laboratory, the same laboratory used for ACTU studies. This procedure was followed for 25 of the 29 subjects. Three subjects had entry data obtained from medical records within the Ohio Health system and exit data collected in the GCRC. One subject's exit blood work was not properly received by the OSU laboratory, thus exit data were subsequently obtained from medical records in Dayton, Ohio.

Radioimmunoassay Procedure. Radioimmunoassay was conducted by trained personnel at The Ohio State University Clinical Research Laboratory using a commercially available salivary cortisol assay kit (Coat-A-Count) from Diagnostic Products Corporation (1997), Los Angeles, California. The Coat-A-Count kit provides a standardized procedure for assay of cortisol in saliva, urine, and plasma and is highly specific for cortisol with extremely low cross-reactivity to other naturally occurring

steroids or therapeutic drugs that may be present in patient samples (Diagnostic Products Corporation, 1997). The investigator was present to assist with the assay procedure. Samples were divided, and three separate assays were completed according to standard OSU laboratory protocol. To assess for inter-assay variation, three subjects had saliva samples included in each assay. Controls (serum pools) with three cortisol levels were assayed as unknowns, and pairs of control tubes were spaced throughout the assay to help verify the absence of significant intra-assay drift. The standardized curves for all three assays were compared, and the inter-assay cortisol measures were evaluated to assure validity of assay outcomes. The detailed procedure used by OSU laboratory personnel is outlined in Appendix D.

Data Analyses

Descriptive Analyses. Means, standard deviations, and distributions are presented at baseline for the demographics of age, education level, employment status, race, and risk factor for experimental and control subjects, and groups were compared for baseline differences on the social support variable. Mean weekly practice time for subjects in the experimental condition was also described. Completers were compared to non-completers on the same data to assess for potential non-completer bias. Means and standard errors are presented for scores on the POMS, MOS-HIV, salivary cortisol levels, CD4+/CD8+ data and viral load, and Health Behavior Checklist. Morning and evening cortisol data were plotted to assess for group differences in degree of diurnal variation. The Symptom Checklist was analyzed to identify those symptoms most

frequently cited as problematic for subjects. Subject use of relaxation and imagery to deal with symptoms is reported.

Inferential Analyses. Each hypothesis was tested using repeated measures ANOVAs to identify group changes for dependent variables. Model assumptions of normality of distribution, homogeneity of variance, and sphericity were tested for each ANOVA. This study hypothesizes a Group by Time Interaction for the key dependent variables. The repeated measures ANOVA model accounts for any baseline inequality in reporting Group by Time Interaction results; thus, it was deemed an appropriate statistical model for use in this study (Munro & Page, 1993; Winer, Brown, & Michaels, 1991). Significant findings were subjected to Dunnett's and Tukey's for post hoc analysis. Dunnett's clarified which timeframes (weeks 2 to 6, 2 to 10, 2 to 14) contributed to the significant finding, and Tukey's confirmed that baseline group differences did not account for the results. Data interpretation considered protocol or drug changes, significant life stressors such as loss of significant other, and infectious illness that may have occurred during the study.

Statistical Software. Data for the MOS-HIV, POMS, Symptom Checklist, SSQ6, and weekly practice were scanned in a verified using the Teleform 6.0 software used at the GCRC. Salivary cortisol, immunological, and health behavior data were entered directly into the SPSS (Version 8.0) and verified by the researcher. All data analyses were completed using the SPSS software. The Power Analysis and Sample Size for Windows (PASS Version 6.0) software (Hintze, 1996) was used for all post hoc

power calculations. Statistical personnel in The Ohio State University Biometrics Laboratory assisted with and verified all statistical computations.

CHAPTER 4

ANALYSIS OF THE DATA

Introduction

This chapter presents the results of data analysis for subjects who participated in the study. A total of 40 subjects were enrolled. Eleven subjects dropped out of the study (27% drop out rate), leaving a total sample of 29 subjects. The first section presents an analysis of dropout rates and potential bias between those subjects who completed the 12-week relaxation protocol and non-completers. Next, descriptive statistics are provided to compare the 18 experimentals and 11 controls (29 completers) at baseline on the demographics of age, education level, employment status, sex, race, risk factor, and social support. Finally, the findings for each research hypothesis are presented. Analyses of the hypotheses are based on the data from the sample of 29 subjects (18 experimental and 11 control) who completed the 3-month protocol.

Assessment of Dropout and Potential Bias from Non-Completers

A sample size of 30 was projected, and 40 subjects were enrolled to allow for subject attrition. A 2:1 experimental to control ratio was established to ensure adequate numbers of experimental subjects. Twenty-seven subjects were randomly assigned to the experimental group, and 18 of these subjects completed the 12-week protocol

(67%). Thirteen subjects were assigned to the control condition, and 11 of these subjects completed the 12-week control period (84%). Thus, 11 subjects withdrew from the study, leaving a total sample of 29 (18 experimental and 11 control). Demographic data for the completers and non-completers were compared to assess for differential characteristics between the two groups (Table 3).

Variable	Completers (n = 29)		Non-completers (n = 11)		p-value
	n	%	n	%	
Age Group					.438
25-34	5	17	4	36	
35-44	15	52	4	36	
45-54	9	31	3	29	
Education					.535
8-12	7	24	3	27	
12+	10	35	6	55	
Undergraduate	7	24	2	18	
Graduate	5	17	0	0	
Employment					.054
Full-time	4	14	5	45	
Part-time	6	21	0	0	
None	19	65	6	65	
Sex					.696
Female	4	14	1	10	
Male	25	86	10	90	
Risk Factor					.115
Homosexual	16	55	10	91	
Bisexual	3	10	0	0	
Heterosexual	10	35	1	9	
Race					1.000
Non-White	6	21	2	18	
White	23	79	9	82	

Table 3. Summary of Demographic Variables for Completers and Non-Completers (Fisher's Exact)

Subjects ranged in age from 25 to 53 years with an average age of 40.1 ($SD = 6.89$) in the completer group and 38.6 ($SD = 6.86$) in the non-completer group. Differences between the completer and non-completer groups were tested using contingency tables. Because of the small number of observations per cell, chi-square assumptions were not met, and the Fisher's Exact statistic was chosen. As noted in Table 3, no significant differences were found for subjects who completed the protocol versus non-completers on the variables of age group, sex, race, education, and risk factor. One variable, employment status, did approach significance ($p = .054$) with 45% of the non-completers engaged in full-time employment versus 13.8% of the completer group. This may have influenced the decision for withdrawal; however, 55% of the non-completers were unemployed, and employment was not given as a reason for withdrawal during exit interviews.

Of the 9 subjects who dropped out of the experimental group, 5 dropped out between the 4th and 6th week. One subject moved, two started new jobs, two started back to school, and one had a drug relapse. In addition, three subjects became ill and decided they would not be able to continue. One subject dropped out of the control condition because a partner became ill, and the second subject (control) stated he was "too anxious" to wait. Overall, no systematic differences were observed in comparing completers to non-completers.

Description of the Sample and Comparison of Demographic Variables by Experimental and Control Group

The sample of 29 subjects who completed this study ranged in age from 25 to 51 years with an mean age of 42 ($SD = 5.54$) for the experimental group and 38 ($SD = 6.89$) for the control group. Most of the subjects were white homosexual males with some college education. Most of the subjects were not employed, and those subjects who were employed were primarily working on a part-time basis. The sample included individuals from black and Hispanic racial groups, and both sexes were represented. The Fisher's Exact statistic was used to assess for baseline differences between the experimental and control group on the demographics of age group, education, employment status, sex, race, and risk factor. No group differences were found for demographic variables (Table 4).

Variable	Experimental (n = 18)		Control (n = 11)		p-value
	n	%	n	%	
Age Group					.405
25-34	2	11	3	27	
35-44	9	50	6	55	
45-54	7	39	2	18	
Education					.868
8-12	4	22	3	27	
12 +	6	33	4	36	
Undergraduate	4	22	3	27	
Graduate	4	22	1	9	
Employment					.738
Full-time	3	17	1	9	
Part-time	3	17	3	27	
None	12	67	7	64	
Sex					.696
Female	2	11	2	18	
Male	16	89	9	82	
Risk Factor					.477
Homosexual	9	50	7	64	
Bisexual	3	17	0	0	
Heterosexual	6	33	4	36	
Race					1.000
Non-White	3	17	3	27	
White	15	83	8	73	

Table 4. Summary of Demographic Variables for Experimental and Control Subjects (Fisher's Exact)

Because social support directly and indirectly influences health behavior, quality of life, neuroendocrine, and immune function (Cacioppo, 1992; Cohen et al., 1992; Glaser-Glaser et al., 1986, 1987a; Malarkey et al., 1994; Unicho et al., 1992)—the dependent variables of interest in this study—experimental and control groups were compared at baseline on the SSQ6. Both experimental and control subjects reported having a mean of 5 ($SD = 2.4$) people upon whom they could depend for support when needed. Additionally, average satisfaction with social support was measured as

somewhat satisfied for both groups on a scale that ranged from very dissatisfied to very satisfied. A t-test of baseline scores showed no significant group differences ($p = .81$) in overall level of support.

Analysis of Training Completion Rate

Of the original 29 subjects randomized to the experimental group, 67% completed training ($n = 18$). Five wait-list control subjects (45%) were subsequently able to complete the 6-month commitment required for training. Six subjects (55%) did not complete the training. The wait-list controls dropped out for several reasons. Two subjects had an increase in symptoms, requiring hospitalization; one subject returned to school; one moved; and one gave no reason.

Analysis of Practice Time for Experimental Subjects

All subjects who participated in the relaxation training agreed to practice the exercises for a minimum of 15 minutes per day, 5 days per week. Each subject recorded the outcomes of practice on a Practice Log that was introduced during the first training session. One log was provided for each week of training, and subjects reviewed practice outcomes with the investigator during regularly scheduled training sessions.

Analysis of practice logs for the experimental group showed that subjects were generally able to achieve their weekly practice requirement. Subjects practiced a mean number of 5 days per week. Total mean practice time over the 12-week program was 120 minutes per week ($SD = 71$ minutes) or 25 minutes for each of the 5 days

($SD = 10$), and practice ranged from 0 to over 8 hours per week. While interrupted practice schedules occurred for several subjects, no subject had more than a 2-week period without recorded practice. For example, one subject had a death in the immediate family and suspended practice that week. Repeated measures ANOVA of mean practice time for weeks 2 to 14 showed no significant differences between weeks ($p = .92$). Overall, analysis showed that subjects did meet the minimum practice requirement required for participation. Because previous research suggests that relaxation practice is relevant to neuroendocrine and behavioral outcomes, this verification of practice time is important for interpretation of study hypotheses.

Analysis of Study Hypotheses

Results of the repeated measures ANOVAs are reported for each of the 5 study hypotheses. Hypothesis testing was restricted to a comparison of the 18 experimental and 11 control subjects for whom full data were available. Distributions of total scores for the two groups were tested on each repeated measures ANOVA for the assumptions of normality, equality of group variance, and sphericity. The Huynh-Feldt adjustment was used to report significance levels for scales that did not meet the sphericity assumption.

Research Hypothesis 1

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in psychological distress.

Psychological distress was operationalized as the mean scores at weeks 2, 6, 10, and 14 on the POMS total and scores for each of the 6 POMS subscales. Repeated measures ANOVAs were conducted on POMS total scores and subscale scores to test for Group, Time, and Group by Time Interaction (treatment) effects (Table 5).

Study Week	Experimental	Control
2	45.8 (10.4)	25.5 (13.4)
6	26.0 (9.4)	22.7 (12.1)
10	21.9 (8.1)	26.6 (10.4)
14	17.6 (8.7)	32.9 (11.1)

Table 5. Mean (SE) POMS Total Scores for Experimental and Control Subjects

POMS Total.

Mean scores on the POMS decreased from weeks 2 to 14 for the experimental group from 45.8 (SE = 10.4) to 17.6 (SE = 8.7), while mean scores for the control group increased from 25.5 (SE = 13.4) to 32.9 (SE = 11.1) on week 14, as illustrated in Figure 2. This trend suggests that experimental subjects experienced a reduction in overall distress over the 14-week period of relaxation training. The major drop in distress scores appeared to occur at week 6, after one month of practice. While overall scores dropped for experimental subjects, average differences between experimental and control subjects over the four measurement periods were not statistically significant for

Group ($p = .94$), Time, ($p = .36$), or Group by Time Interaction ($p = .16$), and the null hypothesis could not be rejected. Data from analysis of the total POMS measure did not support Hypothesis 1. Lack of power (.36) may have contributed to nonsignificant findings for the hypothesized treatment effect.

Figure 2. Plot of Mean POMS Total Scores for Experimental and Control Subjects

POMS Subscales.

Mean and standard error data for the six POMS subscales are presented in Table 6. Only one subscale, Tension-Anxiety, showed significant results. The Tension-Anxiety subscale showed a main effect for Time [$F(3,81) = 2.6$, $p = .05$] with a decrease in both experimental and control mean scores over the 12-week protocol. The hypothesized Group by Time Interaction did not manifest ($p = .20$); thus, although experimental mean scores decreased from 11.5 to 5.2, the change cannot be attributed to

the relaxation intervention. Lack of sufficient power (power = .31) to detect treatment differences may have contributed to the inconclusive finding.

Variable	Experimental Mean (SE)	Control Mean (SE)
Tension/Anxiety		
Week #2	11.6 (2.1)	8.1 (2.6)
Week #6	7.4 (2.0)	8.5 (2.6)
Week #10	6.0 (1.6)	6.7 (2.1)
Week #14	5.2 (1.7)	7.6 (2.2)
Depression/Dejection		
Week #2	16.3 (2.6)	9.3 (3.4)
Week #6	11.5 (2.7)	9.6 (3.4)
Week #10	11.2 (2.2)	10.1 (2.8)
Week #14	9.7 (2.3)	11.5 (2.9)
Anger/Hostility		
Week #2	14.8 (3.0)	9.2 (3.9)
Week #6	9.5 (2.6)	7.2 (3.4)
Week #10	8.3 (1.8)	7.5 (2.4)
Week #14	7.6 (2.2)	10.6 (2.8)
Fatigue/Inertia		
Week #2	12.8 (1.6)	9.5 (2.0)
Week #6	10.3 (1.4)	9.8 (1.8)
Week #10	10.3 (1.7)	11.8 (2.0)
Week #14	9.7 (1.5)	10.2 (1.9)
Vigor/Activity		
Week #2	13.8 (1.5)	14.2 (2.0)
Week #6	15.4 (1.3)	15.5 (1.7)
Week #10	16.4 (1.5)	13.0 (1.9)
Week #14	16.6 (1.4)	12.0 (1.9)
Confusion/Bewilderment		
Week #2	4.3 (1.3)	3.1 (1.7)
Week #6	2.8 (1.2)	3.1 (1.6)
Week #10	2.6 (1.1)	3.5 (1.4)
Week #14	2.1 (1.2)	4.9 (1.6)

Table 6. Mean (SE) Scores of POMS Subscales for Experimental and Control Subjects

Dunnett's post hoc analysis showed that the decrease in experimental subject scores for the Tension-Anxiety subscale was significantly different from baseline to

week 10 ($p < .05$), while no single time point significantly contributed to the decrease in control subject scores. The time effect found for the Tension-Anxiety subscale is shown in Figure 3.

Figure 3. Plot of Tension Anxiety Subscale

Analyses of the remaining 5 subscales were similar to those of the overall POMS. Scores were suggestive of reduced stress for experimental subjects compared to controls; however, results were not significant. Experimental group scores for 4 of the subscales decreased—Depression-Dejection, Anger-Hostility, Fatigue-Inertia, and Confusion-Bewilderment—while scores for these subscales for the control group increased. Whereas scores for experimental subjects on the Vigor-Activity subscale increased (the desired direction of effects), control subject scores decreased. Graphs of mean scores for each of these subscales are shown in Appendix E. Analyses of the

overall POMS and all 6 subscales showed a consistent pattern, suggesting that distress scores were moving in the hypothesized direction for experimental compared to control subjects. This pattern, despite the lack of adequate power, suggests that relaxation techniques may affect several different areas of psychological distress and supports the need for study of relaxation as a useful intervention.

Research Hypothesis 2

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in quality of life.

Quality of life was operationalized as the total MOS-HIV scores at weeks 2, 6, 10, and 14 as well as each of the 11 subscale scores. Mean and standard error data are provided in Table 7.

Study Week	Experimental Mean (SE)	Control Mean (SE)
2	60.78 (17.5)	63.35 (12.7)
6	64.57 (19.6)	62.74 (17.1)
10	66.60 (20.3)	61.24 (18.0)
14	67.94 (18.4)	61.27 (16.1)

Table 7. Mean (SE) MOS-HIV Total Scores for Experimental and Control Subjects

MOS-HIV Total.

Over the 12-week study period, experimental mean scores increased, while mean scores for the control group decreased, suggesting movement in the hypothesized direction. Mean data are illustrated in Figure 4. The repeated measures ANOVA,

however, was not significant for Group ($p = .65$), Time ($p = .73$) or Group by Time Interaction ($p = .29$). Therefore, the null hypothesis was not rejected, and Hypothesis 2 was not supported from the data.

Mean MOS-HIV scores in this sample were higher than those reported for other studies. Wu et al. (1997) reported a baseline mean of 37.7, indicating the sample had higher quality of life scores than did other HIV seropositive groups, and this may have contributed to the lack of significant findings. A difference of only 7.2 points on the MOS-HIV was observed from baseline to week 14, compared to the 22.2 point (1 SD) difference hypothesized in the sample size calculations. Post hoc power calculations indicated much less power for this analysis (power = .25) than the a-priori projected power of .80.

Figure 4. Plot of Mean MOS-HIV Scores for Experimental and Control Subjects Study

MOS-HIV Subscales.

Mean and standard error data for the 11 MOS-HIV subscales are presented in Table 8. To more clearly compare various dimensions with different response formats, subscale data were linearly transformed to a 0 to 100 scale, with 0 indicating the lowest and 100 indicating the highest possible score as recommended in the scoring guidelines. Untransformed data were also analyzed for three separate subscales to ensure that transformation did not affect statistical significance or power. The results reported below are based on the linearly transformed scores.

The hypothesized AVOVA results for only 2 of the 11 MOS-HIV subscales were significant. A significant treatment effect was found for the Role Function subscale, and the Health Transition subscale was significant for Group. Analysis of the remaining 9 subscales showed that experimental group scores increased for every subscale (Appendix F). Control group mean scores showed improvement on 3 of the remaining 9 subscales. Thus, experimental subjects showed consistent improvement on all 11 subscales, but results were not significant. Additionally, experimental group improvement on the Mental Health and Cognitive Function subscales approached statistical significance.

Variable	Experimental Mean (SE)	Control Mean (SE)
Overall Health		
Week #2	48 (6.7)	48 (8.6)
Week #6	51 (7.0)	46 (9.0)
Week #10	56 (6.7)	44 (8.6)
Week #14	58 (6.0)	45 (7.7)
Cognitive Function		
Week #2	73 (5.9)	77 (7.5)
Week #6	82 (4.6)	74 (5.8)
Week #10	80 (5.7)	76 (7.3)
Week #14	84 (4.9)	75 (6.3)
Role Function		
Week #2	50 (10.8)	55 (13.8)
Week #6	44 (11.4)	59 (14.6)
Week #10	53 (10.6)	45 (13.5)
Week #14	56 (9.9)	41 (12.7)
Social Function		
Week #2	58 (4.7)	56 (6.0)
Week #6	59 (5.9)	53 (7.6)
Week #10	63 (6.4)	53 (8.2)
Week #14	62 (5.9)	62 (7.5)
Physical Function		
Week #2	73 (5.7)	69 (7.3)
Week #6	73 (5.5)	67 (7.1)
Week #10	71 (6.8)	71 (8.8)
Week #14	74 (6.4)	70 (8.2)
Mental Health		
Week #2	57 (5.2)	71 (6.7)
Week #6	71 (4.6)	71 (5.9)
Week #10	74 (4.3)	71 (5.6)
Week #14	74 (4.0)	69 (5.1)
Pain		
Week #2	62 (5.3)	74 (6.8)
Week #6	64 (5.1)	72 (6.5)
Week #10	69 (5.3)	70 (6.8)
Week #14	64 (5.9)	69 (7.5)
Vitality		
Week #2	49 (4.3)	48 (5.8)
Week #6	53 (5.1)	50 (6.9)
Week #10	55 (5.2)	47 (6.9)
Week #14	57 (4.8)	44 (6.4)

Table 8 continued

Table 8 continued

Variable	Experimental Mean (SE)	Control Mean (SE)
Health Distress		
Week #2	78 (5.5)	81 (7.0)
Week #6	81 (5.0)	81 (6.4)
Week #10	83 (5.9)	79 (7.6)
Week #14	82 (5.6)	80 (7.2)
Quality of Life		
Week #2	61 (4.1)	61 (5.2)
Week #6	65 (5.4)	64 (6.9)
Week #10	67 (5.3)	66 (6.8)
Week #14	69 (5.7)	68 (7.2)
Health Transition		
Week #2	60 (4.6)	57 (5.8)
Week #6	68 (5.6)	52 (7.1)
Week #10	63 (5.4)	52 (7.0)
Week #14	67 (5.1)	52 (6.6)

Table 8. Mean (SE) MOS-HIV Subscale Scores for Experimental and Control Subjects

Role Function Subscale. Role Function refers to the effect of health on ability to work at a job, do housework, or go to school. A significant Group by Time Interaction [$F(2.3,81) = 4.2$; $p = .01$] was found for this subscale. Thus, this subscale result supports the hypothesized treatment effect. Experimental group scores decreased from baseline through week 6, then increased from weeks 2 to 14 with mean scores of 50 ($SE = 10.8$) and 56 ($SE = 9.9$), respectively at weeks 2 and 14 (Figure 5). Control group scores decreased consistently from a mean of 55 ($SE = 13.8$) at baseline to a mean of 41 ($SE = 12.7$) at week 14.

Dunnett's post hoc analysis was conducted to determine which week(s) contributed to the significant change in outcome. Pairwise comparisons of experimental means between weeks 2 to 6, 2 to 10, and 2 to 14 were not significant, suggesting a gradual increase in mean scores over the entire 12-week program for experimental

subjects. The change in control mean scores, however, was significant from baseline to week 14 ($p = <.05$), suggesting that the decrease in control scores was contributing to the ANOVA result. Because experimental mean scores increased and the repeated measures ANOVA was significant for Group by Time Interaction, these data suggest that relaxation training may improve one's ability to work more productively. However, because control mean scores significantly decreased from week 2 to week 14, this finding warrants further investigation.

Figure 5. Plot of Mean Role Function Scores for Experimental and Control Subjects

Health Transition Subscale. A main between-groups effect was found for Health Transition [$F(1,27) = 5.1$; $p = .03$]. This subscale measures a change in perceived mental and physical health status over each 4-week time period. Tukey's post hoc analysis revealed that experimental and control subjects were not significantly different

at baseline ($p > .05$), suggesting that something had occurred that led to the significant repeated measures ANOVA group effect.

Dunnett's post hoc analysis of the within-group change for experimental and control subjects was not able to detect significant differences from baseline to week 6, weeks 2 to 10, or 2 to 14, suggesting experimental group scores gradually improved and control group scores gradually decreased over the 12-week program. The greatest improvement in experimental group mean scores had occurred by week 6. While findings should be interpreted with reservation, the main group effect and the gradual increase in experimental scores suggest that relaxation may have contributed to the increase in perceived mental and physical health status for experimental subjects; however, this cannot be concluded from the data (Figure 6).

Figure 6. Plot of Mean Health Transition Scores for Experimental and Control Subjects

Mental Health Subscale. The Mental Health subscale, a measure of overall well being, showed a significant Group by Time Interaction [$F(3,81) = 2.7$; $p = .05$] on unadjusted ANOVA analysis; however, this subscale did not remain significant after the Huynh-Feldt sphericity adjustment [$F(1.8,81) = 2.7$; $p = .07$]. Results are addressed because they approached significance for treatment, even though statistical power was low (.23) and because this pattern is consistent with the positive trends suggested by POMS data. The Mental Health subscale results are shown in Figure 7.

Figure 7. Plot of Mean Mental Health Scores for Experimental and Control Subjects

This specific item refers to how much of the time a person has felt anxious, blue, depressed, happy, or peaceful over each previous 4-week period. Experimental scores at baseline were lower with mean scores of 57 ($SE = 5.2$) versus 71 ($SE = 6.7$) for control subjects. Week 14 experimental mean scores increased to 74 ($SE = 4.0$), and

control scores remained relatively unchanged with a mean of 69 ($SE = 5.1$). Thus, experimental subjects showed an improvement in mental health over the 14-week study period compared to control subjects, and the major increase appeared to occur by week 6.

Dunnett's post hoc analysis confirmed this effect, inasmuch as the change in experimental scores from weeks 2 to 6 was significant at $p < .01$. Changes in experimental scores from weeks 2 to 10 and 2 to 14 remained significant. This post hoc analysis also revealed that control group scores were not significantly different from weeks 2 to 6, 2 to 10 or 2 to 14. Tukey's post hoc analysis did not detect baseline differences for experimental and control subjects ($p > .05$). While Group by Time Interaction was not significant, the significant increase in experimental mean scores from baseline through week 14, in the absence of significant change for control subjects, suggests that relaxation may have contributed to the improved mental health scores for experimental subjects. The outcome warrants further study. Because of the nature of the questionnaire, it is not possible to determine if overall mental health for experimental subjects improved because of decreased negative affect (blue, anxious), increased positive affect (calm, happy) or changes in both aspects of mood.

Cognitive Function Subscale. Cognitive Function refers to problem-solving, decision-making, focus of attention, concentration, and forgetfulness. Experimental subjects showed an observable increase during the relaxation practice period with a mean of 73 ($SE = 5.9$) at baseline and a mean of 84 ($SE = 4.9$) at week 14. Scores for control subjects remained relatively stable with a mean of 77 ($SE = 7.5$) and 75

($SE = 6.3$) at weeks 2 and 14, respectively. The major shift in cognitive function appeared to occur after a 1-month practice period (week 6). Mean scores dropped at week 10, then increased again through week 14. This change in experimental scores over time approached significance for a Group by Time Interaction [$F(3,2.0) = 2.5$; $p = .09$] despite the low power. Dunnett's post hoc pairwise analysis revealed that the major increase in experimental group scores occurred by week 6. Experimental group changes were found to be significant from baseline to week 6 and from baseline to week 14 ($p < .05$), indicating these time periods were critical to the ANOVA results. Changes in experimental subject scores between weeks 2 to 10 were not significant, consistent with the observed decrease in scores at week 10 (Figure 8).

Figure 8. Plot of Mean Cognitive Functioning Scores for Experimental and Control Subjects

Thus, analysis of the MOS-HIV total scores and the 11 subscales showed a relaxation treatment effect for only one subscale, Role Function. Results of analysis for the remaining 10 subscales showed that experimental subject mean scores improved for each subscale. The consistency of improvement for experimental subject scores and the results of analysis for Health Transition, Mental Health, and Cognitive Function suggest that the relaxation treatment may have contributed to experimental group improvement on these quality of life indicators; however, this cannot be concluded from the data.

Research Hypothesis 3

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant decrease in AM and PM salivary cortisol levels.

Salivary cortisol was collected (AM and PM) for each subject at weeks 2 (baseline) 6, 10, and 14. One control subject was excluded from the analysis because the equality of variance assumption was not met. Cortisol levels for that subject were well above the available standards in the Coat-A-Count kit; thus, the measures could not be considered as valid.. Subsequent to the data collection, this subject was diagnosed with a possible pituitary or other neuroendocrine disorder that could significantly alter cortisol levels. With this subject excluded, the assumption of equality of variance was met. The mean and standard error data are presented in Table 9.

Study Week		Experimental Mean $\mu\text{g/dl}$ (SE)	Control Mean $\mu\text{g/dl}$ (SE)
AM			
	2	.422 (.158)	.300 (.201)
	6	.453 (.126)	.137 (.161)
	10	.327 (.048)	.215 (.062)
	14	.448 (.089)	.193 (.114)
PM			
	2	.057 (.016)	.088 (.020)
	6	.122 (.050)	.122 (.062)
	10	.062 (.027)	.157 (.033)
	14	.082 (.025)	.134 (.031)

Table 9. Means (SE) Scores for AM and PM Salivary Cortisol Levels for Experimental ($n = 17$) and Control ($n = 11$) Subjects

All AM and PM samples for the relaxation and control group were collapsed into morning and evening values to assess for diurnal variation (Figure 9). The graph illustrates the characteristic peak of cortisol during the morning and the nadir of levels during the evening. Mean AM cortisol level for the experimental group across all time points ($n = 67$ samples) was .393 ($SE = .038$) compared to .303 ($SD = .051$) for controls ($n = 38$ samples). The comparable PM level for experimental subjects was .087 ($SE = .012$) compared to .130 ($SE = .016$) for control subjects. AM salivary cortisol levels (both groups combined) ranged from 2.7 to .04 $\mu\text{g/dl}$, and PM values ranged from .87 to .10 $\mu\text{g/dl}$.

Figure 9. Plot of Mean AM-PM Cortisol Levels for Experimental and Control Subjects

Repeated measures ANOVAs were conducted on salivary cortisol levels to determine if the experimental group had significantly lower AM and PM cortisol levels compared to the control group after participating in the 12-week relaxation program. AM cortisol levels indicated no significant Group ($p = .18$), Time ($p = .62$) or Group by Time Interaction ($p = .48$). Similarly, PM cortisol levels did not significantly differ for Group ($p = .18$), Time ($p = .40$), or Group by Time Interaction ($p = .43$). Thus it was not possible to reject the null hypothesis, and Hypothesis 3 was not supported. Low statistical power for both AM (power = .32) and PM (power = .23) samples may have contributed to the results. Graphs illustrating salivary cortisol levels for experimental and control subjects are in Appendix G.

Research Hypothesis 4

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit a significant increase in CD4+/CD8+ T-lymphocyte ratio and a significant decrease in viral load.

CD4+ and CD8+ cell numbers, CD4+/CD8+ ratios, and viral load data were collected at study weeks 2 and 14. Repeated measures ANOVAs indicated a significant Group by Time Interaction for the CD4+ T-lymphocyte dependent variable [$F(1,27) = .54$; $p = .028$], suggesting experimental group CD4+ counts improved after participating in the relaxation protocol. No significant results were found for CD8+ cell counts, or the CD4+/CD8+ ratio. However, after review of the raw data, two subjects were dropped from the analysis because the assumption of homogeneity of variance was not met. One subject (experimental) had changed antiretroviral medication 4 weeks into the study, which could have affected exit CD4+ counts. The second subject (control) was treated as an outlier with CD4+ helper cell counts of 1 and 2, counts well below values of other subjects included in the analysis. After these adjustments, CD4+, CD8+, and viral load data met the homogeneity of variance assumption. The CD4+ dependent variable remained significant for adjusted scores, and CD8+ and ratio data remained nonsignificant. The mean and standard error scores excluding these two subjects are presented in Table 10.

Study Week	Experimental (SE)	Control Mean (SE)	Normal Values
CD4+			
2	478.06 (23.13)	466.80 (30.16)	320-1900
14	561.18 (23.13)	434.60 (30.16)	
CD8+			
2	1114.00 (68.93)	839.60 (89.87)	150-1000
14	1200.82 (68.93)	988.50 (89.87)	
Ratio			
2	.52 (.03)	.47 (.04)	0.9-3.5
14	.55 (.03)	.47 (.04)	
Viral Load			
2	1308.11 (548.15)	3966.30 (714.69)	0
14	1871.47 (548.15)	4508.63 (790.12)	
Viral Load Log			
2	2.79 (.119)	3.05 (.273)	0
14	2.82 (.119)	3.51 (.172)	

Table 10. Mean (SE) CD4+ and CD8+ cells/mm³, CD4+/CD8+, Viral Load RNA Copies/ml for Experimental (n = 17) and Control (n = 10) Subjects

CD4+ T-Lymphocyte Count. After excluding two subjects from analysis, the Group by Time Interaction [$F(1,25) = 4.6$; $p = .042$] for CD4+ counts remained evident, suggesting the interaction effect was a result of treatment, the 12-week relaxation protocol. Dunnett's pairwise post hoc comparisons showed the increase in CD4+ cells from baseline to week 14 was significant at $p < .05$ for experimental subjects, but the baseline to week 14 decrease was not significant for controls. Additionally, Tukey's analysis showed that experimental and control subject CD4+ scores were not statistically different from each other at week 2, supporting the ANOVA results (Figure 10).

Figure 10. Plot of Mean CD4+ T-lymphocyte Helper Cells/mm³ for Experimental and Control Subjects

CD8+ Absolute Count and CD4+/CD8+ Ratio. Analyses of CD8+ suppressor cells and the CD4+/CD8+ ratio did not show significant group differences. Given the significant CD4+ results, several factors may have contributed to lack of significance in CD4+/CD8+ ratio scores. First, the mean increase in CD8+ cell counts for experimental subjects may have reduced ratio values, even though CD4+ cell counts increased for those subjects. Second, CD8+ cell counts for both groups showed more variability than CD4+ cell counts, and this variability may help to account for lack of significance. Finally, post hoc power analysis was consistently low for CD8+ and ratio data (power = .07). Graphs illustrating CD8+ cell numbers and CD4+/CD8+ ratio changes are shown in Appendix G.

Viral Load. Experimental and control subjects showed a relatively stable viral load, probably reflecting inclusion criteria used for the study. Baseline mean viral load

scores, measured in RNA copies/ml, were higher and showed more variability in the control group. Additionally, an increase in mean viral load copies/ml was observed for week 2 to 14 for both experimental and control groups. Repeated measures ANOVA indicated no significant Group ($p = .19$), Time ($p = .41$), or Group by Time Interaction ($p = .98$) for this measure.

Because of variability in the data and mean baseline differences between the experimental and control groups, viral load log-transformed data were analyzed. The increase in viral load scores represented only a .03 log increase in the experimental group, whereas control group scores increased by .46 log. Repeated measures ANOVA of log data showed a significant main effect for Group [$F(1,26) = 4.8$; $p = .037$]; thus, experimental and control subjects were significantly different for this dependent variable using log transformed data (Figure 11).

Figure 11. Plot of Mean Log-Transformed Viral Load Scores for Experimental and Control Subjects

Dunnett's post hoc analysis of log transformed data showed that the experimental group mean increase in viral load from week 2 to 14 was not significant; however, the increase from baseline to week 14 was significant ($p < .05$) for control subjects. Furthermore, Tukey's post hoc test showed that baseline log viral load mean scores were not different for the two groups; thus, baseline differences did not account for the observed group effect. While log viral load scales increased in both groups, the baseline to week 14 differences were significant only for control subjects. Stability in viral load RNA copies/ml is important for interpretation of cellular immune data, and these results suggest that the significant CD4+ treatment effect observed in this study must be interpreted with caution. The observed decrease in control subject CD+ cell counts may reflect the significant increase in mean viral load observed for that group. Based on the significant group differences found for log viral load data, the significant treatment effect found for CD4+ data cannot be interpreted conclusively. However, the post hoc analysis of CD4+ data showing a significant increase from baseline to week 14 and the stable viral load for experimental subjects suggest that additional research to illuminate the effects of relaxation on cellular immune data is warranted. Results of analysis for CD+, CD8+, and viral load data did not support rejection of the null hypothesis; therefore, Hypothesis 4 was not supported.

Research Hypothesis 5

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in health behavior.

The Health Behavior Checklist used for this study relied on self-report to provide data for 6 major health behaviors, including nutrition, aerobic exercise, alcohol consumption, tobacco use, quality of sleep, and compliance with medication regimen. To obtain an overall health behavior rating, data were scored on a 0 to 1 scale with 0 indicating negative health behavior and 1 indicating positive health behavior. Positive health behavior was defined as meeting or exceeding generally recommended standards for a specific behavior (U.S. Department of Health and Human Services, 1995, 1998), and negative health behavior was defined as inability to meet the recommended standard. An overall Health Behavior rating was obtained by summing the 6 individual scores for each subject. Table 11 provides a brief summary of behavioral standards used for scoring. The specific instrument adapted for this study and detailed scoring criteria are found in Appendix A.

Behavior	Behavioral Standard 0 < Standard ... 1 ≥ Standard
Aerobic activity	15 minutes of aerobic exercise or more 3 times weekly
Alcohol	One serving per day or less
Compliance	Consistently adheres to prescribed HIV regimen
Nutrition	Complete and balanced diet on average weekly
Sleep	7-9 hours of restful sleep on average weekly
Tobacco	Does not currently smoke

Table 11. Behavioral Standards Used as Scoring Guideline for Self-Reported Health Behaviors

Health behavior data were collected and reviewed with subjects according to the 4-week data collection schedule outlined above. Any change in behavior over a 4-week period and use of relaxation to support positive behavioral change was discussed with subjects during regularly scheduled training. The 6 categories of behavior were analyzed descriptively at baseline (Table 12), and the results are presented in context of subject discussions regarding their specific concerns.

Behavior	Standard	Experimental (<u>n</u> = 18)	Control (<u>n</u> = 11)
Alcohol	Met standard	17 (94%)	11 (100%)
	Below standard	1 (6%)	0 (0%)
Compliance	Met standard	17 (94%)	10 (91%)
	Below standard	1 (6%)	1 (10%)
Exercise	Met standard	3 (17%)	2 (18%)
	Below standard	15 (83%)	9 (82%)
Nutrition	Met standard	6 (33%)	4 (36%)
	Below standard	12 (67%)	7 (63%)
Sleep	Met standard	13 (72%)	5 (45%)
	Below standard	5 (28%)	6 (55%)
Tobacco	Met standard	9 (50%)	9 (82%)
	Below standard	9 (50%)	2 (18%)

Table 12. Frequency of Self-Reported Health Behaviors at Baseline (Week 2) for Experimental and Control Subjects

Compliance. Overall compliance (experimental 94% and control 91%) with the HIV medication regimen was found to be consistently strong for all subjects. This result is not surprising, inasmuch as study entry criteria required a stable viral load and achieving such stability can be expected only when the medication regimen is adhered to closely.

Alcohol. Alcohol was used by most subjects; however, use appeared limited to one alcoholic beverage per day or less. Thus, 94% of the experimental and 100% of the control met or exceeded the criteria for this variable. Many subjects actually reported alcohol use as less than once per month. Alcohol intake greater than the defined standard has been reported as a factor that can influence immune response to stress (Glaser-Glaser & Glaser, 1988; Zeller, McCain, McCann et al., 1996). This finding is also not surprising, based on the entry criteria that excluded subjects with current drug abuse, including alcohol.

Nutrition. Adequate nutritional intake was compromised for this sample. Many subjects attempted to supplement their food intake with nutritionally complete supplements and over-the-counter medications. However, by self-report, only 6 (33%) of the experimental subjects and 4 (36%) of the controls reported they met adequate nutritional standards. Most of the subjects considered nutrition an important health behavior; however, ability to maintain a completely balanced diet was problematic for a several reasons, including symptoms of nausea associated with HIV medications, lack of appetite, severe diarrhea, food intolerance, and lack of financial resources.

Exercise. Adequate exercise was also problematic for most subjects, although most did consider exercise an important priority for continued stress management and health improvement. Baseline scores showed that only 3 (17%) experimental and 2 (18%) control subjects were able to achieve 15 minutes of aerobic exercise 3 times per week. Some subjects reported great difficulty in regular exercise participation because of extreme fatigue, neuropathy in the legs and feet, pain, nausea, and other physical

symptoms. Social isolation, fear that exercise might lead to weight loss, and poor financial resources were also cited as barriers to adequate exercise.

Tobacco. Tobacco use, an addictive behavior, was somewhat problematic for 11 of the 29 subjects (50% of experimental subjects and 18% of control subjects reported current tobacco use). Generally, subjects who smoked reported use as less than one pack of cigarettes daily. Most of these subjects were actively trying to decrease tobacco use. Most of the subjects who did not currently smoke previously had been smokers. Marijuana use was not included in the definition of tobacco, as only 2 subjects reported occasional use of marijuana and only for medicinal purposes.

Sleep. Ability to achieve 7 to 9 hours of restful sleep was reported by 72% of experimental and 45% of control subjects; however, difficulty in achieving restful sleep was also common in both groups. Five experimental (28%) and 6 control (55%) subjects reported averaging 5 or less hours of sleep per night. Individual sleep disturbances varied among subjects, and most subjects reported that their sleeping difficulty contributed to fatigue and overall increased stress levels.

Total Health Behavior. Mean and standard error data for experimental and control subjects are presented in Table 13. Analyses in Total Health Behavior summed scores were obtained using the repeated measures ANOVA. Results showed a significant Group by Time Interaction for total scores [$F(2.5,81) = 4.7$; $p = .008$ after the Huynh-Feldt sphericity adjustment]; thus, the null hypothesis was rejected. Experimental subjects showed significant improvement in health behavior compared to control subjects over the 12-week training intervention.

Study Week	Experimental Mean (SE)	Control Mean (SE)
2	3.61 (.110)	3.72 (.141)
6	4.11 (.110)	3.54 (.141)
10	3.77 (.110)	3.90 (.141)
14	4.16 (.110)	3.63 (.141)

Table 13. Mean (SE) Health Behavior Total Scores for Experimental and Control Subjects. Higher scores indicate more positive health behavior.

Figure 12 illustrates the variability observed in self-reported health behavior scores over the 12-week measurement period. Tukey's post hoc analysis confirmed Group scores were not significantly different at baseline, supporting the observed treatment effect. Dunnett's post hoc analysis was conducted to determine which specific measurement point(s) were most significant for the behavioral outcome. The experimental group showed a significant change ($p < .01$) between weeks 2 to 6 and again between weeks 2 to 14. Differences in scores from week 2 to 10, however, were not significant. For control subjects, differences in scores from weeks 2 to 6, 2 to 10, and 2 to 14 were not significant. Thus, the improvement in experimental subject scores was achieved by week 6 but not sustained at week 10. By week 14, scores had improved again.

Figure 12. Plot of Mean Total Health Behavior Scores for Experimental and Control Subjects

The data suggest that over time, relaxation may be an important factor contributing to more positive health behavior and behavior change, and this interpretation was supported by subject verbal report. For example, one subject, who considered alcohol use a major stressor, quit drinking alcohol by week 14. While alcohol intake was not a problem for most of the subjects in this sample, it was for this individual. Several other subjects reported a decreased use of alcohol. Five subjects began an exercise program or increased the amount of weekly exercise to meet recommended standards. Two of these subjects stated that the increased exercise was directly related to a decrease in HIV-related symptoms. Several subjects reported increased awareness and attention to the diet, and 4 subjects reported that relaxation was a major factor contributing to longer or more restful sleep.

Symptom Self-Report and Use of Relaxation for Symptom Management

The 20-item General Symptom Checklist was analyzed to provide additional insight into quality of life and behavioral issues for people living with HIV. The type and frequency of HIV-related symptoms measured by this instrument reflect several of the areas measured by the MOS-HIV and POMS instruments. Data were analyzed descriptively and were used to expand findings related to the major hypotheses.

The mean number of symptoms reported by experimental subjects at baseline was 6.6 (SD = 3.12); control subjects reported similar scores with a mean of 8.5 (SD = 3.57) symptoms per subject. Table 14 provides a summary of 15 symptoms that were reported as troublesome by at least 20% of subjects at baseline.

Symptom	Experimental Group (n = 18)		Control Group (n = 11)	
	Frequency	%	Frequency	%
Fatigue	16	89	10	83
General Pain	13	72	3	25
Numbness of Extremities	13	72	4	33
Diarrhea	11	61	5	42
Gas	11	61	9	50
Forgetfulness/Trouble Concentrating	9	50	9	75
Headache	7	39	7	58
Decreased Sex Drive	5	28	3	25
Heartburn	5	28	4	33
Nausea	5	28	6	50
Difficulty breathing	4	22	4	33
Numbness in Lips/Mouth	4	22	4	33
Thrush	4	22	3	25
Vomiting	4	22	2	17

Table 14. Number and Percent of Symptoms Most Frequently Reported by Experimental and Control Subjects at Baseline (Week 2)

HIV-Related Symptoms. Fatigue and forgetfulness or trouble concentrating were the two symptoms frequently reported as interfering with daily life. During entry interview and relaxation training sessions, subjects often described the severe and debilitating nature of their fatigue. Difficulty in concentrating on task completion was also reported as a major stressor for many subjects.

Gastrointestinal disturbance was also frequently reported. Specific symptoms included severe diarrhea, nausea with or without vomiting, gastric distension and heartburn, and a change in taste with daily food intake. These symptoms were primarily discussed as being related to the anti-retroviral or other medication required for treatment of HIV. Most of the gastrointestinal symptoms were considered extremely stressful and often were reported to interfere with general food intake. Managing to balance the rigorous medication schedule with dietary intake was reported as extremely stressful by most of the subjects.

Physical pain was a third general symptom area reported by subjects as particularly problematic. Types of pain included nonspecific general muscle sensitivity and soreness, as well as neck, leg, and general abdominal discomfort. Specific pain symptoms included severe peripheral neuropathy in the legs and feet, joint pain in the hips, headache, and frequent migraine. Subjects who reported pain discussed the limiting nature of daily activity related to their symptoms. Overall, peripheral neuropathy, general pain, and severe fatigue were cited as major factors that limited physical activity and employment.

Relaxation and Symptom Management. The General Symptom Checklist also provided a measure of relaxation and imagery use for symptom management. For those subjects who identified symptoms as particularly stressful, the training protocol was modified to incorporate general relaxation management methods. For example, if pain was found to interfere with a subject's ability to relax, the specific protocol was modified slightly until the subject was able to practice the technique and achieve a relaxation response as measured by skin temperature and verbal report.

Data for those subjects in the experimental group who reported symptoms were analyzed to determine the percentage of subjects who were actively using relaxation and imagery for symptom management over the 12-week protocol. With the exception of two experimental subjects who had previously received some relaxation training, no experimental subject reported use of relaxation and imagery at baseline. At the end of training, subjects reported use of relaxation methods in dealing with numerous HIV-related symptoms. Table 15 shows the use of relaxation techniques for those subjects who reported symptoms. Only data for which 50% of subjects reported effective symptom management by week 14 are reported. These data suggest that subjects who reported HIV-related symptoms were able to use relaxation techniques for 9 of the 15 most frequently cited areas of functioning, and the technique should be considered important as a symptom management tool.

Symptom	Study Week			
	2	6	10	14
Fatigue ($\underline{n} = 16$)	12.5	87	93	79
Pain ($\underline{n} = 13$)	15	100	90	82
Numbness ($\underline{n} = 13$)	8	25	63	80
Forget ($\underline{n} = 9$)	11	40	50	60
Headache ($\underline{n} = 7$)	0	44	100	75
Nausea ($\underline{n} = 5$)	0	75	100	80
Sex ($\underline{n} = 5$)	0	25	50	50
Breath ($\underline{n} = 4$)	25	100	100	100
Vomiting ($\underline{n} = 4$)	0	0	25	50

Table 15. Use of Relaxation and Imagery for Symptom Management by Experimental Subjects Reporting Symptoms

This chapter presented findings for the sample of 18 experimental and 11 wait-list controls subjects that participated in the 12-week relaxation program. First, potential bias from non-completers was considered. Second, experimental and control subjects were compared on the demographics of age, education, employment status, sex, race, risk factor, and social support; no significant differences were found. Third, analysis of practice time for the experimental group was presented to validate subject participation. Finally, findings were presented for each of the 5 study hypotheses and the General Symptom Checklist.

CHAPTER 5

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Introduction

A repeated measures design was used to test the effectiveness of a 12-week relaxation and guided imagery program in a randomized sample of 18 experimental and 11 control subjects diagnosed with HIV-1 on indicators of stress and quality of life. Outcomes of psychological, neuroendocrine, and behavioral changes that occurred as individuals with this chronic illness regularly participated in relaxation practice were compared with those of individuals who did not participate. The study framework was based on a biobehavioral model of adjustment to chronic stress, which posits that the psychological distress and reduced quality of life frequently associated with chronic stress negatively impact cellular immunity via neuroendocrine pathways and changes in health behavior. These biologic effects may negatively influence long-term health outcomes (Anderson et al., 1994). Table 16 summarizes the results, and conclusions are presented in order of the five hypotheses that were tested.

Hypotheses	Dependent Variable	Measure	Effect
Hypothesis 1	Psychological Distress	POMS Total 6 subscales	Total: ns* Tension-Anxiety: Time Others: ns*
Hypothesis 2	Quality of Life	MOS-HIV Total 11 subscales	Total: ns* Role Function: Interaction (.01) Health Transition: Group Others: ns*
Hypothesis 3	HPA axis	Salivary Cortisol	ns
Hypothesis 4	Disease Marker	CD4+/CD8+ Viral Load	CD4+ cell: Interaction Others: ns Log scale: Group Others: ns
Hypothesis 5	Behavior	Health Behavior	Total: Interaction (.008)

*ns improvement in experimental scores compared to controls

Table 16. Summary of Significant Findings based on Repeated Measures ANOVA

Research Hypothesis 1

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in psychological distress.

For the purpose of this study, psychological distress was defined as a state of negative emotional affect or mood and was measured by the POMS, a 65-item questionnaire that is sensitive to changes associated with brief interventions (Haskell et al., 1969; McNair et al., 1992).

No interaction effects were found for total mood disturbance or any of the psychological distress variables measured on the 6 POMS subscales; thus, the relaxation training did not appear to significantly reduce psychological distress compared to controls, and Hypothesis 1 was not supported. However, the consistent increase in scores observed for experimental subjects, congruence with data gathered

from the symptom checklist, and low statistical power suggest that ongoing study of relaxation effects on overall stress levels and psychological distress in general deserves further investigation. While findings were not significant, several conclusions can be drawn from the data.

First, analysis of POMS scores suggests subjects in this study were not acutely distressed. Mean scores in the sample were much lower than those previously reported for acutely distressed samples—patients diagnosed with malignant melanoma, undergoing bone marrow transplant, and recent HIV+ diagnosis (Fawzy et al., 1990a). Scores were also comparable to standardized scores reported for healthy, non-stressed adults (McNair et al., 1992). Thus, positive improvement on the POMS measure might be expected to occur gradually and may have been difficult to detect by week 12. Mulder et al. (1994) reported significant improvement on comparable POMS scores in HIV+ subjects who participated in a 15-week cognitive-behavioral stress management program. However, Fawzy et al. (1990a, 1990b) found significant group differences in patients with malignant melanoma participating in a 6-week stress management program for vigor only. Significant group differences in depression, confusion, fatigue, and total mood did not emerge until the 6-month measurement period. Thus, moderate distress levels and low statistical power may have contributed to the lack of significant findings.

Second, even though statistical significance was not achieved, experimental subject mean scores for all 6 subscales and total mood disturbance showed a consistent trend of movement in the hypothesized direction. Depression, anxiety, anger, fatigue,

and confusion decreased for experimental subjects, and vigor increased. Less distress for control subjects was found for the tension subscale only. This subscale showed significant tension reduction for both experimental and control subjects.

A growing body of evidence suggests stress management, including relaxation, appears to modify psychological distress and the effects of stress on immune function (Antoni et al., 1990; Fawzy et al., 1990a, 1990b; Kiecolt-Glaser & Glaser, 1992; LaPerriere et al., 1990; Mulder et al., 1994; Spiegel, Bloom, & Yalom, 1989a, 1989b). Fawzy et al. (1990a, 1990b) and Spiegel, Bloom, Kraemer, and Gottheil (1989) suggested that long-term change in total mood, and vigor, in particular, is associated with greater longevity in the cancer population. Given this growing body of research and the importance of psychological distress suggested by the Biobehavioral Model, the consistent trends found on POMS data in this study suggest that ongoing study of relaxation in the HIV+ population is warranted.

Psychological distress in HIV+ subjects has been found to directly correlate with symptomatology in several studies (Coleman & Holzemer, 1999; Hays, Turner, & Coates, 1992; Linn, Monnig, Cain, & Usch, 1993). McCain and Zeller (1996) suggested that measurement of psychological distress is often confounded with somatic symptoms, and these variables should be treated separately, especially with respect to immune parameters. In this study, data from the General Symptom Checklist were consistent with POMS trend data for 3 subscales—fatigue, vigor, and confusion. Fatigue and forgetfulness were frequently reported by both experimental and control subjects. By week 14, 79% of those reporting fatigue and 60% reporting forgetfulness

were using relaxation and imagery for symptom management. These data provide additional support to the conclusion that ongoing investigation of relaxation as a method to attenuate or buffer psychological distress is warranted in the HIV+ population.

Research Hypothesis 2

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in quality of life.

The MOS-HIV quality of life measure used in this study was developed specifically for people diagnosed with HIV; thus, the results of data analysis may be particularly relevant for this population. A significant treatment effect was found for only 1 of the 11 MOS-HIV subscales analyzed. Overall quality of life scores found in this study were much higher than projected for determination of sample size (Wu et al., 1997) and were found to be comparable to MOS-HIV scores reported for asymptomatic, Stage I, and Stage II HIV+ subjects (Burgess, Dayer, Catalan, Hawkins, & Gazzard, 1993; Gillespie, 1997; Wu et al., 1997). High MOS quality of life scores were consistent with the POMS data, suggesting moderate psychological distress. As with POMS data, moderate scores and low statistical power may have contributed to the lack of significant findings on this population-specific quality of life measure. Post hoc power analysis, using mean and standard error data obtained from both instruments, suggests that 42 subjects per group would be needed to detect differences with a statistical power of .80 for these data in future studies (Hintz, 1996).

The significant interaction effect found on the Role Function subscale, to the best of this investigator's knowledge, has not been reported previously in stress management literature for the HIV+ population. MOS-HIV role function was defined as the ability to achieve in one's role, through work, volunteer activity, school, or other means. The significant treatment effect is consistent with findings on the POMS for increased vigor and decreased inertia. Data from a phenomenological study of HIV+ men and women reported 9 themes associated with feelings of self-worth and emotional well-being (Coward, 1994). Three of the 9 themes included taking care of self, having hope, and having purpose or making a difference. Thus, ability to perform meaningful work appears to be an important quality of life factor for HIV+ subjects, and the significant finding for role function in this study warrants further exploration.

The significant group effect for the health transition subscale showed that subjects did improve on this measure of perceived mental and physical health status. This finding cannot be interpreted as an effect of the relaxation program; however, there was improvement. Change in perceived health appears congruent with increased ability to complete meaningful work found on the role function subscale and is consistent with the nonsignificant yet positive trends observed for experimental subjects on the POMS scales. Additionally, post hoc data analysis for the health transition subscale showed that the experimental group change occurred gradually over the entire 12-week program, a finding that could reflect increasing use of relaxation for symptom management, particularly pain and fatigue. These convergent data lend some support to

the suggestion that relaxation may have contributed to the group effect observed on the health transition subscale.

While the remaining MOS-HIV scores did not show significant results, the data do show a consistent positive improvement within the experimental group, suggesting that quality of life increased. Scores for the mental health and cognitive functioning subscale approached significance for a treatment effect. Mean scores on all other subscales—overall health, social function, physical function, vitality, health distress, quality of life, and pain—improved for the experimental group. No consistent pattern was observed in control data. As with the trend data found on the POMS, this should not be interpreted to infer causality; however, findings from this study suggest that relaxation training may contribute to improved quality of life for subjects who actively practice the techniques.

Results of this study are limited with respect to interpreting effectiveness of relaxation to enhance coping in the HIV+ population. Subjects in this study did not appear to be severely distressed, and quality of life was not low. Nonetheless, subjects participated, practiced, and reported on their practice for three months. This may suggest that subjects were motivated by factors other than stress and psychological distress. The consistent reduction in distress (POMS) and increased quality of life (MOS-HIV) observed for experimental subjects may suggest that relaxation contributes to a positive state of well-being for people who are not particularly distressed. Positive emotional states in HIV+ subjects are associated with positive coping strategies, including cognitive reappraisal, problem-focused coping, spiritual beliefs and practices,

and infusing ordinary events with positive meaning. This “existential well-being” has been found to be predictive of psychological well-being as measured by reduced depression and anxiety (Coleman & Holzemer, 1999). Furthermore, positive emotional states have been found to coexist with emotional distress in HIV+ bereaved men (Folkman, 1997).

The MOS-HIV mental health subscale measures emotional well-being. Experimental group scores improved for this subscale, and the change approached significance for a treatment effect, suggesting that subjects may have achieved more positive emotional states after participating in the program. McCain et al. (1996) found significantly improved emotional well-being on the Functional Assessment of HIV Infection in a sample of HIV+ subjects immediately after participating in a 6-week relaxation and guided imagery intervention. Fawzy et al. (1990a) found significant improvement in vigor after a 6-week program for cancer patients. These data lend some support to the suggestion that relaxation and imagery may be useful in promoting positive states of well-being for people with chronic illness.

Absence of psychological distress (negative affect) does not equal presence of well-being (positive affect). Absence of distress is a neutral emotional state. A preponderance of PNI research focused on the effect of objective stress, psychological distress, and reduced quality of life on immune competence and disease progression. While ongoing study of these psychophysiological relationships is critical, the question of intensifying overall states of positive well-being for people who not particularly distressed has not been extensively addressed. Most of the studies that have

investigated psychological well-being have been correlational and have not included physiological disease state variables (Holzemer & Wilson, 1995; McCain & Zeller, 1996).

Experimental group scores on the cognitive functioning subscale improved, and the change approached significance for a treatment effect. This subscale provides a measure reflecting problem-solving, decision-making, concentration, and forgetfulness. Cognitive focusing skills are required for psychophysiological relaxation, and subjects frequently cited increased “ability to concentrate,” “feeling less scattered,” “less mind-racing,” and “feeling more clear” as immediate benefits of relaxation practice. Additionally, forgetfulness or difficulty concentrating was reported by 50% of experimental and 75% of control subjects, and relaxation was used to deal with this symptom. Findings on the cognitive function subscale are supported by those of McCain et al. (1996), who found that weekly relaxation practice significantly correlated with higher quality of life, more frequent use of problem-focused coping, less avoidant thinking, and less uncertainty. Based on the findings from the present study, it can be suggested that future longitudinal studies of the benefits of relaxation investigate more directly the roles that relaxation and imagery have in supporting emotional states of well-being, positive coping processes, and perhaps immune competence in the HIV+ population.

Research Hypothesis 3

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit a significant decrease in AM and PM salivary cortisol levels.

Differences in AM and PM salivary cortisol levels over the 12-week protocol were not observed in this study, showing that relaxation practice did not decrease HPA axis activity as hypothesized. This finding has several possible implications for future studies of relaxation in the HIV+ population.

Normal diurnal variation was observed, and the wide range of AM and PM values observed in this sample is characteristic of individual variability seen in normal controls (Kahn, Rubinow, Davis, Kling, & Post, 1988). These findings support the validity of the salivary cortisol measurements in this study. Mean AM and PM cortisol levels for both experimental and control subjects were within a range that is considered usual for non-acutely stressed people with no evidence of HPA axis dysfunction (Enwonwu, Meeks, & Sawiris, 1996; Kahn et al., 1988; Norbiato et al., 1997; Tarui & Nakamura, 1987). The normal levels of cortisol observed in this sample are consistent with findings on the MOS-HIV and POMS instruments, suggesting that subjects were not highly distressed. Additionally, scores were comparable to those recently reported in a similar sample of subjects, which found no decrease in cortisol levels for experimental subjects compared to controls after a 12-week exercise intervention (Gillespie, 1997).

The hypothesized effect for cortisol was based on an assumption that the long-term stress of HIV+ status would be reflected in higher basal cortisol levels; thus, given the more normal cortisol levels found in this study, it is possible that the 12-week study period was not long enough to detect group differences. In a relaxation and biofeedback study of 13 breast cancer survivors, Gruber et al. (1993) noted no significant change in plasma cortisol until after 6 months. Future studies should consider periodic monitoring of cortisol activity over a much longer period.

While basal cortisol levels in this sample appeared to be normal, this conclusion cannot be confirmed in the absence of other neuroendocrine measures. HPA axis dysfunction is frequently reported in the HIV+ population, and subjects were screened for preexisting neuroendocrine disease; however, interpretation of cortisol was limited in this study because other neuroendocrine data were not collected. The various mechanisms underlying HPA axis dysfunction in HIV are not well understood. Approximately 50% of HIV non-AIDS subjects have been shown to have normal HPA axis function. However, 25% appear to have HPA axis dysfunction with elevated basal cortisol, and 25% present with HPA axis dysfunction associated with normal basal cortisol (Azar & Melby, 1993; Norbiato et al., 1997). Additional neuroendocrine measures such as ACTH and CRH production could help to more precisely measure cortisol-stress relationships and thus the relationship between relaxation therapy and HPA axis function. Future relaxation research measuring salivary cortisol should, at minimum, differentiate subjects with HIV from those with AIDS and ARC and require more stringent medical screening for preexisting neuroendocrine disease.

The accumulating body of research on chronic stress and its effect on autonomic, neuroendocrine, and immune relationships has greatly benefited from use of an acute stress model (Cacioppo et al., 1995; Kiecolt-Glaser & Glaser, 1992). Ongoing research of relaxation on the cortisol-stress response would appear to benefit from use of healthy subjects and the acute stress paradigm. Additionally, relaxation has been hypothesized to reduce physiological sympathetic arousal, perhaps through its effect on parasympathetic tone (Benson, 1975; Sakakibara et al., 1994); thus, catecholamine levels, heart rate variability, and other measures of sympathetic nervous system reactivity might be useful to advance the body of research dealing with physiological effects of relaxation and other forms of stress management on these systems.

Research Hypothesis 4

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in CD4+/CD8+ ratio and significant decrease in viral load.

The hypothesized treatment effects on CD4+/CD8+ ratio and viral load disease state markers were not found in this study. Additionally, interpretation of the significant treatment effect found for CD4+ counts remains inconclusive because of the relationship of CD4+ cells to viral load. The significant increase observed in experimental CD4+ cells compared to controls is supported by evidence from other stress management research showing positive changes in CD4+ counts (Antoni, Baggett et al., 1991; Gruber et al., 1993; McCain & Zeller, 1996; Ruzyla-Smith et al., 1995) as

well as consistent and positive effects on other cellular immune markers (Kennedy et al., 1990; Kiecolt-Glaser & Glaser, 1991; Rood, Bogaards, Goulmy, & Houwelingen, 1993; Zachariae et al., 1997). Experimental subjects exhibited stable mean viral loads as measured by RNA copies/ml and log-transformed scale. Within-group post hoc analysis showed that the increase in CD4+ cell counts from baseline to week 14 was significant. Thus, the significant increase in experimental CD4+ counts should not be minimized.

However, collection and interpretation of CD4+/CD8+ and viral load data for this study had numerous limitations. First, there was no control for diurnal variation. Second, four subjects had data obtained from laboratories outside of the primary laboratory system used for this study. Third, there was no control for type of anti-retroviral viral medication or length of time on the medication regimen (Zeller, McCain, & Swanson, 1996). Fourth, there was no control for HIV+ versus AIDS diagnosis. Fifth, only one baseline sample was used to assess change, and two measurement occasions do not accurately reflect CD4+ activity (Kiecolt-Glaser & Glaser, 1988). Additionally, viral load log data showed significant group differences between experimental and control subjects, and post hoc analysis revealed that the group difference was accounted for by a significant increase in control subject viral load levels from baseline to week 14. Thus, the CD4+ results obtained in this study cannot be interpreted as evidence that relaxation practice can increase CD4+ cell counts. Regular practice of relaxation and guided imagery may contribute to stability in CD4+ cell counts for some HIV+ individuals who are compliant with the prescribed medication

regimen and have a stable viral load; however, much more evidence is warranted before this assertion can be made.

No significant differences were found for CD8+ cell counts, and interpretation of this finding is difficult. CD4+ helper lymphocytes and CD8+ suppressor lymphocytes do not necessarily vary in a linear relationship, and it is possible that a longer time period would be needed to observe CD8+ changes. Additionally, the cells have different cellular immune functions (Calabrese et al., 1987; Zeller, McCain, & Swanson, 1996), and it is possible that a decrease in CD8+ cells might not be appropriate for a given viral load. The ability to quantify viral load is a recent advancement, and the relationship of CD4+ and CD8+ count to different viral load levels continues to be an important area of investigation (Zeller, McCain, & Swanson, 1996).

Several research questions are proposed for the ongoing investigation of relationships between relaxation and cellular immune data. First, CD4+ cell counts do not reflect an accurate measure of CD4+ T-lymphocyte function, and the actual clinical significance on possible long-term disease outcomes related to CD4+ cell count changes remains unanswered (Kiecolt-Glaser & Glaser, 1992). Second, in psychophysiological research the concepts of individual response specificity and individual response variability require examination (Cacioppo & Berntson, 1992; Cacioppo & Tassinary, 1990). While mean experimental group CD4+ cell counts significantly increased, within the experimental group, CD4+ data showed individual variability. CD4+ counts did not increase for all experimental subjects. This observation raises the question of

how individual response variability in other physiological systems—such as differences in sympathetic or cardiovascular reactivity—might influence the relaxation to CD4+ outcome. Individual variability in autonomic reactivity (Cacioppo et al., 1995; Kiecolt-Glaser & Glaser, 1992) and HPA axis function (Kusnecov & Rabin, 1994; Norbiato et al., 1997) have been shown to influence the effect of acute stress on immune function. The same is possible for stress management techniques such as relaxation. Third, the amount of ongoing practice that would be needed to sustain an increased CD4+ cell count is unknown. Kiecolt-Glaser et al. (1985) found that that immune changes associated with relaxation practice, in a sample of geriatric subjects, were not sustained once practice was discontinued; thus, prospective longitudinal studies may be important to understanding the possible benefits of long-term relaxation practice. Fourth, given that salivary cortisol levels in experimental and control subjects were not significantly different in this sample, the issue of general physiological mechanism(s) mediating a change in immune parameters is also an important issue for future research. Other neuroendocrine systems, specifically neuropeptides, have been suggested as responsive to relaxation and imagery (Kiecolt-Glaser & Glaser, 1991; Kiernan, Dane, Phillips, & Price, 1995; Pert, Ruff, Weber, & Herkenham, 1985).

Research Hypothesis 5

In comparison to untrained HIV seropositive subjects, HIV seropositive subjects who regularly practice relaxation will exhibit significant improvement in health behavior.

To this investigator's knowledge, relaxation studies in the HIV+ population have not included measurement of health behavior. Given that the Biobehavioral Model clearly identifies health behavior as a major variable or pathway influencing immune reactivity and long-term disease outcomes, the inclusion of these data is a strength of this study. Experimental subjects showed a significant improvement on total health behavior scores compared to control subjects as hypothesized.

Although this finding is important, the results must be interpreted with some reservation. The Health Behavior Checklist used in this study used a nominal scale for measurement of behavior. Future study of health behavior would be improved by the addition of more refined measurements, including physical data, to validate self-reports. Differentiating addictive behavior (i.e., tobacco and alcohol use) from non-addictive behavior (i.e., diet and exercise) would also help to clarify the relationship between relaxation training and promotion of positive health behavior versus addiction recovery.

Lack of ability to meet healthy standards of behavior, particularly diet and exercise, appeared to be a source of stress for several subjects in this sample. Given their underlying disease process, subjects were aware of the importance of positive health behavior for disease management. Subject use of relaxation and imagery to deal with symptoms of severe gastrointestinal distress, fatigue, and pain may have been an important factor contributing to the significant behavioral improvement observed in the experimental group.

Future relaxation protocols for HIV+ subjects might be improved by incorporating more direct strategies to deal with illness-related symptoms that influence

an individual's health behavior and quality of life. The use of "complementary" therapy has been positively correlated with severity of disease symptomatology, specifically amount of pain (Ostrow et al., 1997), suggesting that subjects experiencing major symptoms may be particularly willing to adopt relaxation as a symptom management technique. Additionally, McCain and Zeller (1996) suggested that current PNI research in the HIV+ population has not adequately addressed the relationship between disease-related symptoms and quality of life.

The sample of HIV+ subjects in this study may reflect a unique group of individuals predisposed to positive behavior change; therefore, results should not be interpreted as suggesting that relaxation improves health behavior. Subjects appeared to be compliant with their medication regimen and sought to participate in the study to learn techniques they perceived as useful for disease management. In general, all subjects achieved the 5 days/week, 15-minutes/day practice requirement. Because subjects were ready and willing to participate in this program, it is possible they were in a state of readiness for other behavioral change. Lack of information on the relationship between relaxation and health behavior change in people with chronic illness supports the need for ongoing investigation. The interpretation of behavior change in the present study is limited by lack of data regarding health beliefs and readiness for change. Future research would benefit from the use of a theoretical behavior change model (Strecher & Rosenstock, 1997).

Summary

Post hoc analyses of the MOS-HIV mental health, cognitive functioning subscales, the POMS tension/anxiety subscale, and total health behavior suggest another consideration for future research. Given that the largest benefit was detected by week 6 and that there was further benefit derived from relaxation beyond 6 weeks, it can be suggested that future treatment designs incorporate more intensive training for the first 6 weeks and rely on monthly group support efforts to maintain ongoing relaxation behavior beyond 6 weeks. Such a design would decrease the amount of time required for training and increase training intensity at the early stages of treatment, a strategy that might facilitate the conduct of larger studies.

The results of this study show that relaxation and imagery may be important tools for a select group of HIV+ patients in managing disease-related symptoms, specific quality of life issues, and select health behaviors. Relaxation practice may contribute to improved immune system indicators of disease for those subjects who comply with their medication regimens. Relaxation is a relevant, feasible intervention that involves no risk to the participant. The training required is time-limited and resource-sparing and provides an opportunity for the patient to independently and actively participate in his or her own health care. As the incidence of HIV and other chronic illness continues to rise in the next decade, it is critical for health-care professionals to develop a variety of cost-effective interventions that support drug therapy and can enhance individual quality of life and long-term disease outcomes. The

study of relaxation and imagery as interventions in combination with other non-pharmacological interventions is an important area for health promotion research.

Appendix A
Instruments for Data Collection

DEMOGRAPHIC FORM

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11

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Figure 1 consists of two side-by-side line graphs, labeled (a) and (b). Both graphs have 'Percentage of respondents' on the y-axis, ranging from 0 to 100 in increments of 20. The x-axis represents 'Level of agreement' with the statement 'The government should do more to protect the environment', with categories: 'Strongly agree', 'Agree', 'Disagree', and 'Strongly disagree'.

Graph (a) shows the distribution for the 'Control' group. The data points are approximately: Strongly agree (25%), Agree (55%), Disagree (15%), and Strongly disagree (5%).

Graph (b) shows the distribution for the 'Treatment' group. The data points are approximately: Strongly agree (35%), Agree (50%), Disagree (10%), and Strongly disagree (5%).

Age Group: ☐ 18-24

© 25-34

03544

045-54

O 55-64

O 65-75

O > 75

Highest Education

○ Some College

○ College Diplomas

○ Advanced Degree

Race: ☒ Black

© White

○ Native Americans

Other

Ethnic background:

● **Non-Allopathic**

☐ YES ☐ NO

0
10

Orientation: ☐ homosexual

☐ heterosexual ☐ bisexual

☐ **Full Time**

○ Part Time

○ Unsetup/Disabled

Occupation: _____

● **Full time**

○ Part Time

○ Not Applicable

Type: _____

Relaxation and Guided Imagery

DEMOGRAPHIC FORM

Medical Insurance:

☐ ☐
yes no

Insurance Source:

- ☐ *Private*
☐ *Public*
☐ *Other*

Date of HIV Diagnosis:

/ /

ACTU Cohort: ☐ *yes*
☐ *no*

How many of your friends know you are HIV+ ?

☐ *None* ☐ *Few* ☐ *Some* ☐ *All*

How many members of your family know you are HIV+ ?

☐ *None* ☐ *Few* ☐ *Some* ☐ *All*

How many of your co-workers know you are HIV + ?

☐ *None* ☐ *Few* ☐ *Some* ☐ *All*

Medical Record Number

(administrative use only)

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
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POMS Inventory

Study Date: - - -

Study Week: Study Number:

Below is a list of words that appear on challenge prompts here. Please read each one carefully. Do not fill in the circles under the number which best describes how you have used FEELING WORDS THE PAST WEEK INCLUDING TODAY. Make sure you have answered every item.

The numbers refer to these phrases:

<p>6 - Not at all 1 - A little 2 - Moderately 3 - Quite a bit 4 - Extremely</p>		<p>6 - Not at all 1 - A little 2 - Moderately 3 - Quite a bit 4 - Extremely</p>	
1. Friendly	☐ ☐ ☐ ☐ ☐ ☐	21. Ignorant	☐ ☐ ☐ ☐ ☐ ☐
2. Nervous	☐ ☐ ☐ ☐ ☐ ☐	22. Misled	☐ ☐ ☐ ☐ ☐ ☐
3. Angry	☐ ☐ ☐ ☐ ☐ ☐	23. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
4. Worried	☐ ☐ ☐ ☐ ☐ ☐	24. Ignorant	☐ ☐ ☐ ☐ ☐ ☐
5. Happy	☐ ☐ ☐ ☐ ☐ ☐	25. Suspicious	☐ ☐ ☐ ☐ ☐ ☐
6. Disoriented	☐ ☐ ☐ ☐ ☐ ☐	26. Nervous	☐ ☐ ☐ ☐ ☐ ☐
7. Lonely	☐ ☐ ☐ ☐ ☐ ☐	27. Nervous	☐ ☐ ☐ ☐ ☐ ☐
8. Confused	☐ ☐ ☐ ☐ ☐ ☐	28. Unable to concentrate	☐ ☐ ☐ ☐ ☐ ☐
9. Nervous for things done	☐ ☐ ☐ ☐ ☐ ☐	29. Focused	☐ ☐ ☐ ☐ ☐ ☐
10. Shaky	☐ ☐ ☐ ☐ ☐ ☐	30. Happy	☐ ☐ ☐ ☐ ☐ ☐
11. Lethargic	☐ ☐ ☐ ☐ ☐ ☐	31. Anxious	☐ ☐ ☐ ☐ ☐ ☐
12. Focused	☐ ☐ ☐ ☐ ☐ ☐	32. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
13. Nervous for things done	☐ ☐ ☐ ☐ ☐ ☐	33. Suspicious	☐ ☐ ☐ ☐ ☐ ☐
14. Shaky	☐ ☐ ☐ ☐ ☐ ☐	34. Nervous	☐ ☐ ☐ ☐ ☐ ☐
15. Lethargic	☐ ☐ ☐ ☐ ☐ ☐	35. Focused	☐ ☐ ☐ ☐ ☐ ☐
16. Focused	☐ ☐ ☐ ☐ ☐ ☐	36. Nervous	☐ ☐ ☐ ☐ ☐ ☐
17. Nervous	☐ ☐ ☐ ☐ ☐ ☐	37. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
18. Shaky	☐ ☐ ☐ ☐ ☐ ☐	38. Anxious	☐ ☐ ☐ ☐ ☐ ☐
19. Lethargic	☐ ☐ ☐ ☐ ☐ ☐	39. Focused	☐ ☐ ☐ ☐ ☐ ☐
20. Focused	☐ ☐ ☐ ☐ ☐ ☐	40. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		41. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		42. Unable to concentrate	☐ ☐ ☐ ☐ ☐ ☐
		43. Focused	☐ ☐ ☐ ☐ ☐ ☐
		44. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		45. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		46. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		47. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		48. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		49. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		50. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		51. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		52. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		53. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		54. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		55. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		56. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		57. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		58. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		59. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		60. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		61. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		62. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		63. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		64. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		65. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		66. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		67. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		68. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		69. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		70. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		71. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		72. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		73. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		74. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		75. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		76. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		77. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		78. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		79. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		80. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		81. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		82. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		83. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		84. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		85. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		86. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		87. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		88. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		89. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		90. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		91. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		92. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		93. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		94. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		95. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		96. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		97. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		98. Nervous	☐ ☐ ☐ ☐ ☐ ☐
		99. Disoriented	☐ ☐ ☐ ☐ ☐ ☐
		100. Nervous	☐ ☐ ☐ ☐ ☐ ☐

Relaxation and Guided Imagery Study

MOS-III Health Survey

Study Week

Study Number

Study Date

 - -

Instructions: The following questionnaire asks about many aspects of your health, how you are feeling and what you are able to do. The form is brief and should take no more than 10 minutes to complete. Each question is in the same general format.

Please note: *Each question should be answered based on your general health over the past 4 weeks.* It is important to answer each question by placing an "x" in the one box that best describes your overall health during the past 4 week time period.

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

2. How much bodily pain have you generally had during the past 4 weeks?

None	Very Mild	Mild	Moderate	Severe	Very Severe
☐	☐	☐	☐	☐	☐

3. During the past 4 weeks, how much did pain interfere with your normal work (or your normal activities, including work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

MOS-HIV Health Survey

(continued)

4. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so how much?

(Check one box on each line)	YES, limited a lot (1)	YES, limited a little (2)	NO, not limited (3)
a) The kinds or amounts of vigorous activities you can do, like lifting heavy objects, running or participating in strenuous sports.	☐ 1	☐ 2	☐ 3
b) The kinds or amounts of moderate activities you can do, like moving a table, carrying groceries or bowling.	☐ 1	☐ 2	☐ 3
c) Walking uphill or climbing (a few flights of stairs).	☐ 1	☐ 2	☐ 3
d) Bending, lifting or stooping.	☐ 1	☐ 2	☐ 3
e) Walking one block	☐ 1	☐ 2	☐ 3
f) Eating, dressing, bathing or using the toilet.	☐ 1	☐ 2	☐ 3

5. Does your health keep you from working at a job, doing work around the house or going to school?

Y	☐
N	☐

MOS-HIV Health Survey

(continued)

6. Have you been unable to do certain kinds or amounts of work, housework, or schoolwork because of your health?

Y ☐
N ☐

For each of the following question, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
1	2	3	4	5	6

7. How much of the time, during the past 4 weeks, has your health limited your social activities (like visiting with friends or close relatives)?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

8. How much of the time, during the past 4 weeks:

a) Have you been a very nervous person?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

b) Have you felt calm and peaceful?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

c) Have you felt downhearted and blue?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

d) Have you been a happy person?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

e) Have you felt so down in the dumps that nothing could cheer you up?

☐	☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

MOS-HIV Health Survey

(continued)

For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

	All of the Time 1	Most of the Time 2	A Good Bit of the Time 3	Some of the Time 4	A Little of the Time 5	None of the Time 6
9. How often during the past 4 weeks:						
a) Did you feel full of pep?	☐	☐	☐	☐	☐	☐
b) Did you feel worn out?	☐	☐	☐	☐	☐	☐
c) Did you feel tired?	☐	☐	☐	☐	☐	☐
d) Did you have enough energy to do the things you wanted to do?	☐	☐	☐	☐	☐	☐
e) Did you feel weighed down by your health problems?	☐	☐	☐	☐	☐	☐
f) Were you discouraged by your health problems?	☐	☐	☐	☐	☐	☐
g) Did you feel despair over your health problems?	☐	☐	☐	☐	☐	☐
h) Were you afraid because of your health?	☐	☐	☐	☐	☐	☐
10. How much of the time during the past 4 weeks:						
a) Did you have difficulty reasoning and solving problems, for example, making plans, making decision, learning new things?	☐	☐	☐	☐	☐	☐
b) Did you forget things that happened recently, for example, where you put things and when you had appointments?	☐	☐	☐	☐	☐	☐
c) Did you have trouble keeping your attention on any activity for long?	☐	☐	☐	☐	☐	☐
d) Did you have difficulty doing activities involving concentration and thinking?	☐	☐	☐	☐	☐	☐

Study Week # _____
Date _____

RS-ID # _____
PID # _____

Health Behavior - Self-Report

I. Nutrition History

1	2	3	4	5
	Notoriously Poor	Somewhat Reduced	Complete & Reduced	
	a	b	c	d

2. Did you ever eat a diet? ☐ yes ☐ no

If YES:
What kind?

3. Did you ever exercise? ☐ yes ☐ no

If YES:
How?

Please complete the attached nutrition check-up.

II. Tobacco Use

4. Have you ever smoked tobacco? ☐ yes ☐ no

If YES:

a. How old were you when you started smoking? _____ years

b. Do you currently smoke tobacco products or use smokeless tobacco? ☐ yes ☐ no

If YES:

(1) How would you classify tobacco use on average per week?

☐ low (≤ 1 pack cigarettes or 2 cigars per week)

☐ mild ($\frac{1}{2}$ pack cigarettes or 1 cigar daily)

☐ moderate (≥ 1 pack cigarettes or 2-3 cigars daily)

☐ heavy (≥ 2 packs cigarettes or 3+ cigars daily)

5. Have you ever smoked marijuana? ☐ yes ☐ no

If YES:

a. Do you currently smoke marijuana? ☐ yes, frequently ☐ yes, occasionally ☐ no

b. How long have you been smoking marijuana? _____ years

6. Have you ever smoked a pipe or a bong? ☐ yes ☐ no

If YES:
How?

Study Week # _____
Date _____

RS-ID# _____
PID# _____

III. Alcohol & Drug Use

If YES:
Specify kind:

If YES:
How?

If YES:

a. How much do you drink on average?

- ☐ ≤ 1 serving/week
☐ 1 serving/day
☐ ≥ 3 servings/day

If YES:
How?

IV. Sleep Behavior

11. How many hours of sleep do you get on average?
0-3 4-6 7-9 10-12 12+
a b c d e

12. How would you describe your sleep?
Restful, wake up feeling refreshed. Somewhat restful, still feel drowsy. Interrupted sleep, not restful.
a b c

If YES:
How?

Study Week # _____
Date _____

RS-ID # _____
PID # _____

V. Physical/Aerobic Activity

IF YES:

How many times per week?

☐ <1 time per week

☐ 1 time per week

☐ 2-3 times per week

☐ 3-4 times per week

☐ 5-7 times per week

☐ >7 times per week

List the activities:

IF YES:

How?

IF YES:

What?

Health Behavior - Self-Report Scoring

Behavior	Behavioral Standard
	0 < Standard ... 1 ≥ Standard
Aerobic activity	15 minutes of aerobic exercise or more 3 times weekly
Alcohol	One serving per day or less
Compliance	Consistently adheres to prescribed HIV regimen
Nutrition	Complete and balanced diet on average weekly
Sleep	7-9 hours of restful sleep on average weekly
Tobacco	Does not currently smoke

Aerobic Activity	< 3-4 times weekly = 0
	≥ 3-4 times weekly = 1
Alcohol	> 1 serving daily = 0
	≤ 1 serving daily = 1
Compliance	Occasionally misses dose = 0
	Regular schedule = 1
Nutrition	a, b = 0
	c, d, e = 1
Sleep	< 7 hours nightly = 0
	≥ 7 hours nightly = 1
Tobacco	yes = 0
	no = 1

RELAXATION AND GUIDED IMAGERY STUDY SOCIAL HISTORY

Study week: Study Number Date - -

The following questions ask about people in your environment who may have provided social support during the past four weeks. Questions 1, 3, 5, 7 and 9 ask about the number of people who provide support in an area. Questions 2, 4, 6, 8 and 10 ask about your overall level of satisfaction with the number of people and quality of support in an area. If you have no support for a question, you would report "none" but still rate your level of satisfaction. Question 11 asks whether or not you have experienced a change in the number or quality of social support. Please answer all questions as best you can. Use the following codes as needed.

SATISFACTION CODES:

1 = Very Dissatisfied 2 = Somewhat Dissatisfied 3 = Somewhat Satisfied 4 = Very Satisfied

1. How many people can you really count on to be dependable when you need help?

none	1-4	5-10	>10
☐	☐	☐	☐
2. How satisfied are you with the support you have in this area?

Use Satisfaction codes			
☐	☐	☐	☐
3. How many people can you really count on to help you feel more relaxed when you are under pressure or tense?

none	1-4	5-10	>10
☐	☐	☐	☐
4. How satisfied are you with the support in this area?

Use Satisfaction codes			
☐	☐	☐	☐
5. How many people accept you totally including your best and worst points?

none	1-4	5-10	>10
☐	☐	☐	☐
6. How satisfied are you with the support have in this area?

Use Satisfaction codes			
☐	☐	☐	☐
7. How many people can you really count on to care about you, regardless of what is happening to you?

none	1-4	5-10	>10
☐	☐	☐	☐
8. How satisfied are you with the support have in this area?

Use Satisfaction codes			
☐	☐	☐	☐
9. How many people can you really count on to help you feel better or console you when you are feeling upset or "down in the dumps"?

none	1-4	5-10	>10
☐	☐	☐	☐
10. How satisfied are you with the support have in this area?

Use Satisfaction codes			
☐	☐	☐	☐
11. During the past 4 weeks, has the number of people who support you changed?

Increased	no change
☐	☐
Decreased	
☐	

Social Support and Life Stress: The questions in this scale ask you about your feelings and thoughts about life stress you may have experienced during the last month. In each case, please indicate your answer by filling in the circle beside the statement that best represents how often you felt or thought a certain way.

12. In the last month, how often have you been upset because of something that happened unexpectedly?

- ☐ never
- ☐ almost never
- ☐ sometimes
- ☐ fairly often
- ☐ very often

13. In the last month, how often have you felt you were unable to control the important things in your life?

- ☐ never
- ☐ almost never
- ☐ sometimes
- ☐ fairly often
- ☐ very often

14. In the last month, how often have you felt nervous and "stressed"?

- ☐ never
- ☐ almost never
- ☐ sometimes
- ☐ fairly often
- ☐ very often

15. In the last month, how often have you felt confident to handle your personal problems?

- ☐ never
- ☐ almost never
- ☐ sometimes
- ☐ fairly often
- ☐ very often

Relaxation and Guided Imagery Study Symptom Review

Study Week: Study Number: Date: - -

Please indicate whether you are currently, or have in the last week experienced any of the following symptoms. If you answer yes to any of the symptoms, indicate the frequency and severity of the symptom and whether or not you were successful in using relaxation or guided imagery to control the symptom.

Symptom	Present?	Frequency	Severity	RGI used?
Change in Taste	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Decreased Sex Drive	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Diarrhea	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Difficulty Breathing	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Dry Heaves/ Wretching	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Fatigue	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Fever	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Forgetfulness/Trouble concentrating	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no

Relaxation and Guided Imagery Study
Symptom Review-cont.

Symptom	Present?	Frequency	Severity	RGI used?
Gas or Distension	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
General Pain	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Headache	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Heartburn	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Nausea, Sick to Stomach	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Night Sweats	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Tingling, Numbness, Pain in Extremities	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Tingling, Numbness, Pain in Lips or Mouth	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no

Relaxation and Guided Imagery Study
Symptom Review-cont.

Symptom	Present?	Frequency	Severity	RGI used?
Skin Rash	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Thrush	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Vomiting	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Weight Loss	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Other	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Other	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no
Other	☐ yes ☐ no	☐ rarely ☐ sometimes ☐ often	☐ mild ☐ moderate ☐ severe	☐ yes ☐ no

PRACTICE LOG

Study Number

--	--	--	--	--

Study Week

--	--

Sunday's Date

		-			-		
--	--	---	--	--	---	--	--

Use this key:

SUN	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

MON	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

TUE	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

WED	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

THU	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

FRI	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

SAT	Number of Times you practiced	0 1 2 3 4 5	Total Time (mins)			Finger Temperature			
	000000								
Did anyone help you practice?			00	Level of Alertness			000000		
Did you feel relaxed?			00	Your Focus of Attention			000000		

PLEASE DESCRIBE YOUR IMAGERY ON THE BACK PAGE.

Appendix B
Forms for Enrollment

ENTRY ASSESSMENT RELAXATION AND GUIDED IMAGERY STUDY

Initials:

RS-ID:

Date of Birth

Support Person:

Date of Diagnosis:

Physician:

ACTU studies:

MEDICAL AND HEALTH HISTORY:

Neuropsychological assessment

Psychiatric diagnosis or tmt within the past 12 months

Anti depressant or anxiolytic drugs

CNS sarcoma, lymphoma

Any disturbance in memory, attention, concentration, planning, oreintation

Physical appearance

Affect and general behavior

Previous hx of HIV CNS involvement

Neurological Assessment (chart review)

Stable viral load (2 or more over past 6 months)

Medications—current treatment started

Antiretrovirals	Antifungals	MAC Prophylaxis
VIRAMUNE (nevirapine)	Mycelex	Mycostatin
Rescriptor (delavirdine)	Nilstat	Biaxin
Epivir (3TC)	Sporomox	Zithromax
Zerit (d4tT)		
Hivid (ddc-zalcitabine)	<u>Antivirals</u>	<u>Antibiotics</u>
Videx (ddl)	Acyclovir	
Retovir (ZDV or AZT)		
Crixivan (indinavir)	<u>PCP Prophalaxis</u>	<u>Antidepressants/Anxiolytics</u>
Invirase (saquinavir)	Dapsone	
Viracept (nelfinavir)	Pentam	
Norvir (ritonavir)		Bactrum/septra

HIV-related symptoms

AIDS diagnosis; date change:

Frequency and type of recent infections/ hospitalization; wasting syndrome; persistent fever

Neuroendocrine involvement:

Overall health rating – good – fair - poor

Nutrition and exercise behavior

Smoking behavior

Financial and Social support

Current major symptoms

EXPECTATONS OF RELAXATION TRAINING

Top 3 life stressors

Program expectations/ training timeframe

Previous use of relaxation or related methods

Use of support person

Value of experimental and control group data

Best times for training

TRAINING GOAL SUMMARY**PROGRESS NOTES**

Subject number _____

Initials _____

Division of Infectious Diseases
425 University Hospital Clinic
436 West 10th Avenue
Columbus, OH 43210-1292
Phone 614-514-1111

AUTHORIZATION FOR RELEASE OF MEDICAL INFORMATION

Patient ID Number _____
Medical Record Number _____

I, _____ hereby authorize The Ohio State University AIDS
Last Name First Name Middle Initial

Clinical Trials Unit, and/or the Infectious Disease Clinic to release and furnish to:

Sharon Scott-Shaffer
Newton Hall - 1505 Neil Avenue
292-8211
Please Specify and Give Address

the following information contained in my outpatient medical and/or research records regarding
my research study participation, medical care and/or treatment:

____ research records only ____ medical records only X both research and medical records

Purpose of Disclosure:

Relaxation and Guided Imagery Research Protocol

I understand and acknowledge that this authorization extends to all or any part of the records
designated above, which may include treatment for physical and mental illness, and/or
alcohol/drug abuse, and or AIDS (Acquired Immunodeficiency Syndrome), and/or may include the
results of HIV test or the fact that an HIV test was performed. I expressly consent to the release of
information designated above. I also understand that this authorization extends to the release of
information via U.S. Mail, overnight mail, telephone or facsimile machine (fax).

This consent is valid for 60 days, unless revoked by my written notice, provided said notice is
received prior to release of the above designated information.

X _____
Signature of Patient or Person Authorized to Consent

Date

X _____
Relationship, if not Patient

X _____
Witness

Date

Appendix C
Relaxation Training Protocol

Relaxation Training Protocol

Week 1 - Enrollment

1. Study criteria and neurological assessment
2. History
3. Subject goals

Week 2 - Training I GCRC

1. Data Collection
2. Relaxation Exercise—Breathing techniques and Centering Exercise & Biofeedback
3. Imagery Exercise—Safe Place
4. Biofeedback methods
5. Handout—Relaxation and Breathing Skills—Achterberg

Week 3 - Training II GCRC

1. Review Practice Log
2. Relaxation Exercise—Breathing and Centering
3. Imagery Exercise—Inner guide or Wise Person
4. Handout—Opening the door to Change—Dossey

Week 4 - Home Visit - Training III

1. Environmental assessment and relaxation rituals
2. Review Practice Log
3. Relaxation Exercise—progressive muscle relaxation
4. Imagery Exercise—HIV and Healing Belief Systems
5. Handout—Imagery in Healing Rituals

Week 5 - Telephone Contact and Support

Week 6 - Training GCRC; Data Collection

1. Data Collection
2. Review Practice Logs
3. Relaxation Exercise—Individualized
4. Imagery Exercise—Dialogue with Symptoms

Week 7 - Telephone Contact and Support

Week 8 - Training GCRC

1. Review of Practice log
2. Relaxation Exercise—Identification & Disidentification
3. General Imagery Exercise—Compromised Immune system or Dialogue with Symptoms

Week 9 - Telephone Contact and Support

Week 10 - Training GCRC; Data Collection

1. Review Practice Logs
2. General Healing Imagery

Week 11 - Telephone Contact and Support

Week 12 - Telephone Contact and Support

Week 13 - Telephone Contact and Support

Week 14 - Training Completion; Data Collection

1. Ongoing imagery rituals
2. Program evaluation

Appendix D
Salivary Cortisol Assay Dilution Procedure

Salivary Cortisol

1. Warm things up

Thaw samples and controls (in box in -20°C freezer) and bring kit components to room temperature.

2. Label tubes

For samples, label coated tubes from kit, 2 per sample

For total counts, label 2 plain tubes TC.

For nonspecific binding, label two plain tubes NSB

Label 2 coated tubes each:

A	B	E	Bio 1
B/4	C	F	Bio 2
B/2	D		Bio 3

3. Dilute Standards and Controls

Label 1 plain tube each, and then dilute according to directions:

Label Tube	Add water	Also add
A	900µl	100µl undiluted A (in vial from kit)
B/4	450µl	450µl of the diluted B/2
B/2	450µl	450µl of the diluted B
B	900µl	100µl undiluted B
C	450µl	50µl undiluted C
D	450µl	50µl undiluted D
E	450µl	50µl undiluted E
F	450µl	50µl undiluted F
Bio 1	450µl	50µl undiluted Bio 1
Bio 2	450µl	50µl undiluted Bio 2
Bio 3	450µl	50µl undiluted Bio 3

4. Set up assay

Follow Coat-A-Count procedure.

Appendix E
POMS Subscales

Figure 13. Depression-Dejection Subscale for Experimental and Control Subjects

Figure 14. Anger-Hostility Subscale for Experimental and Control Subjects

Figure 15. Vigor-Activity Subscale for Experimental and Control Subjects

Figure 16. Fatigue-Inertia Subscale for Experimental and Control Subjects

Figure 17. Confusion-Bewilderment Subscale for Experimental and Control Subjects

Appendix F
MOS-HIV Subscales

Figure 18. Overall Health Subscale for Experimental and Control Subjects

Figure 19. Social Function Subscale for Experimental and Control Subjects

Figure 20. Physical Function Subscale for Experimental and Control Subjects

Figure 21. Pain Subscale for Experimental and Control Subjects

Figure 22. Vitality Subscale for Experimental and Control Subjects

Figure 23. Health Distress Subscale for Experimental and Control Subjects

Figure 24. Quality of Life Subscale for Experimental and Control Subjects

Appendix G

AM-PM Salivary Cortisol Data
CD4+/CD8+ Data
Viral Load Data

Figure 25. AM Salivary Cortisol Levels in Experimental and Control Subjects

Figure 26. PM Salivary Cortisol Levels for Experimental and Control Subjects

Figure 27. CD8+ Suppressor Cells for Experimental and Control Subjects

Figure 28. CD4+/CD8+ Ratio for Experimental and Control Subjects

Figure 29. Viral Load for Experimental and Control Subjects

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