Published in final edited form as:
Psychosom Med. 2008 June ; 70(5): 575–584. doi:10.1097/PSY.0b013e31817a5d30.

The Effects of Psychological Interventions on Neuroendocrine Hormone Regulation and Immune Status in HIV-Positive Persons:

A Review of Randomized Controlled Trials

Adam W. Carrico, Ph.D.[1] and **Michael H. Antoni, Ph.D.**[2,3]

[1]University of California, San Francisco Department of Psychiatry

[2]University of Miami Department of Psychology

[3]University of Miami Department of Psychiatry

Abstract

We reviewed randomized controlled trials (RCTs) that examined the effects of psychological interventions on HIV disease markers including neuroendocrine hormone regulation and immune status. Utilizing both PubMed and PsycINFO, we searched for RCTs published over the past 20 years (1987-2007). Of the 31 RCTs identified, 14 tested effects of psychological interventions on neuroendocrine regulation or immune status. Despite the fact that there are significant methodological limitations of RCTs that have been conducted to date, psychological interventions for HIV-positive persons have been shown to be efficacious in improving psychological adjustment compared with wait-list or treatment as usual control conditions. However, there is little support for differential efficacy of group-based interventions that have been tested to date, even in comparison with semistructured social support groups. Irrespective of the treatment modality, it seems that interventions that are successful in improving psychological adjustment are more likely to have salutary effects on neuroendocrine regulation and immune status. Psychological interventions represent a viable adjuvant treatment that can assist patients with improving psychological adjustment and potentially enhancing immune status. To inform the development of innovative treatments with potentially superior efficacy, deconstruction trials are necessary to examine the effects of distinct components of multimodal psychological interventions compared with nonspecific social support effects. Effectiveness trials of promising psychological interventions with more representative samples of HIV-positive persons are also needed to provide more definitive information on the clinical utility and potential cost-effectiveness of treatments that have been developed to date.

Introduction

It has been well-established that persons with human immunodeficiency virus (HIV) infection have high rates of stressful life events and dysphoria (1). HIV presents individuals with multiple challenges which may overwhelm their coping resources and impair psychological adjustment to the ongoing demands of managing this stigmatized, chronic illness (2,3). Depressive symptoms and stress have been linked to HIV disease progression (4). On the other hand, positive psychological states such as positive affect and finding benefits in living with a chronic illness promote resilience in the face of negative life events, facilitate more effective management of HIV infection, and independently predict less rapid HIV disease progression

Corresponding Author: Adam W. Carrico, Ph.D., University of California, San Francisco, Health Psychology Program, 3333 California St., Suite 465, Box 0848, San Francisco, CA 94143 - 0848, Tel: 415-476-7756, Fax: 415-476-7744, Email: adam.carrico@ucsf.edu.

(5-10). Consequently, psychological interventions designed to improve psychological adjustment (i.e., decrease negative affect as well as enhance positive psychological states) may encourage behavior change, modulate stress physiology, and slow HIV progression (11,12). However, consistent with the broader literature on the effects of psychological interventions on immunity (13), there are significant methodological limitations of the randomized controlled trials (RCTs) that examined the efficacy of psychological interventions on HIV disease markers. The goal of this paper is to review RCTs examining the efficacy of psychological interventions on neuroendocrine hormone regulation and immune status in order to provide recommendations for future research in this area.

Although ongoing monitoring of the T-helper (CD4+) cell count and viral load are part of the standard of care for the medical management of HIV infection, long-term follow-up is often necessary to observe clinically meaningful changes (14). Other measures may provide important information regarding the capacity of the immune system to defend against certain opportunistic infections and cancers. For example, the ability of lymphocytes to multiply when challenged by antigens, evaluated by testing proliferative responses to plant mitogens such as phytohemagglutinin (PHA), may partially compensate for declines in CD4+ cells as HIV progresses (15). It is also noteworthy that individuals with acquired immune deficiency syndrome (AIDS) who remain healthy despite having critically low CD4+ cell counts display a relative preservation of natural killer (NK) cells and natural killer cell cytotoxicity (NKCC), innate immune parameters which are important for the surveillance of pathogens and neoplasias (16). Finally, HIV-positive persons are commonly co-infected with a variety of other viruses that may accelerate HIV replication and directly contribute to the development of AIDS-related conditions (17). Increases in immunoglobulin G (IgG) antibodies indicate decrements in cellular-mediated immune control over latent viral infections such as Epstein-Barr virus (EBV), potentially placing individuals at increased risk for more rapid HIV disease progression (18).

Interventions for HIV-positive persons that successfully improve psychological adjustment may enhance immune status by modulating neuroendocrine hormone regulation (12). Several adrenal hormones—including cortisol and catecholamines—are known to be altered by modifiable psychological factors such as cognitive appraisals and coping responses (19). More effective regulation of neuroendocrine hormones may predict improvements in various indices of immune status that retard the onset of disease complications in HIV-positive persons (20). This is supported by findings indicating that elevated cortisol impairs cellular immunity (21-24) as well as predicts faster progression to AIDS and mortality (25). Other investigations have observed that higher concentrations of norepinephrine (NE) promote *in vitro* elevations in HIV viral load (26), and higher autonomic nervous system activity at rest prior to beginning highly active anti-retroviral therapy (HAART) predicts poorer suppression of HIV viral load and decreased CD4+ cell reconstitution (27).

Utilizing both PubMed and PsycINFO, we searched for randomized controlled trials (RCTs) in HIV/AIDS published over the past twenty years (January of 1987 - June of 2007) with the following key words: adherence, anger, anxiety, bereavement, cognitive-behavioral, coping, depression, intervention, positive affect, relaxation, and stress management. Of the 31 RCTs identified, we focused on the14 that examined psychological intervention effects on neuroendocrine hormone regulation or immune status. These included RCTs of cognitive behavioral, relaxation and meditation, bereavement, and emotional expression interventions (see Table 1).

Cognitive-Behavioral Interventions

A large proportion of psychological interventions for HIV-positive persons employ cognitive-behavioral techniques (28). By promoting enhanced awareness of cognitive appraisals of stressors and teaching cognitive restructuring, cognitive-behavioral therapy improves emotion regulation and reduces maladaptive behaviors (29). Cognitive behavioral stress management (CBSM) is one of the more common of these interventions (30,31). CBSM is a 10-week, group-based intervention that incorporates training in cognitive-behavioral therapy, coping skills, interpersonal skills, and relaxation techniques (progressive muscle relaxation, guided imagery, autogenics, and meditation).

Cognitive-behavioral interventions for HIV-positive persons are efficacious in reducing negative affect when compared to wait-list or treatment as usual controls (32-45). However, cognitive-behavioral treatments for HIV-positive persons have not demonstrated superior efficacy in reducing negative affect compared to other interventions (e.g., interpersonal therapy) or semi-structured social support groups (33,35,46). Overall, cognitive-behavioral interventions that reduce negative affect tend to show improvements in HIV disease markers. In RCTs where cognitive-behavioral interventions were unsuccessful in improving psychological adjustment or where they were compared to other active treatments, no effects on immune status were observed.

RCTs have examined the efficacy of cognitive-behavioral interventions that are tailored to meet the needs of individuals at various points in the experience of HIV infection (e.g., serostatus notification, early emergence of symptoms). In addition to the potential psychological benefits of addressing the unique challenges at distinct stages of HIV infection, RCTs conducted at discrete points in the disease experience may provide insight into the most optimal timeframe(s) where interventions may influence immune status. For example, it is plausible that intervention effects on immune status are more reliably observed among individuals in the earlier stages of HIV infection where the immune repertoire is largely intact and responsive to psychological changes. On the other hand, psychological interventions may also be effective with HAART-treated individuals given the ability of these medications to markedly slow rates of viral replication and immune decrements. The cognitive-behavioral interventions outlined in Table 1 were delivered at various stages of HIV infection. Our discussion of these RCTs will be organized by HIV stage.

Serostatus Notification (Responding to an HIV Seropositive Diagnosis)

In the initial trial of CBSM, gay men who did not know their HIV serostatus were randomized to group-based CBSM, group-based aerobic exercise, or an assessment only control (41,47). After five weeks, men provided blood for HIV antibody testing and were informed of their serostatus 72 hours later. Among HIV-positive men, controls showed significant increases in anxiety and depression, whereas those in the CBSM and aerobic exercise groups reported no changes. HIV-positive men in CBSM displayed significant increases in CD4+ cell counts, NK cells, PHA lymphocyte responses, and NKCC pre to post notification. Controls showed concurrent decrements in NK cell counts, PHA lymphocyte responses, and NKCC (41). Thus, these findings provided some preliminary evidence that psychological interventions could modulate immunologic parameters in parallel with changes in mood even at the very earliest points in the disease process.

Coping with Asymptomatic HIV Infection

The period after HIV serostatus notification can also be stressful despite the absence of overt symptoms as individuals face an unpredictable disease course. Psychological interventions may assist asymptomatic persons in coping with this uncertainty. Cleary and colleagues

examined the effectiveness of a group-based intervention that provided cognitive-behavioral coping skills training to increase social support and promote behavior change in a diverse sample of newly diagnosed blood donors (44). Compared to a community referral control, no intervention effects on depressive symptoms or CD4+ counts were observed at 1-year follow-up. However, only 38% of those randomized to the intervention attended any group sessions. The lack of effects on immune status may be attributable to the fact that this intervention was unsuccessful in reducing depressive symptoms. This is supported by the results of another RCT where no differences in CD4+ cells or T-cell proliferative responses were observed between cognitive-behavioral and supportive-expressive groups that were equally efficacious in reducing distress (33,48). Men in both interventions who reported greater reductions in distress showed smaller CD4+ cell count declines over 2 years (48). In other work, Coates and colleagues examined the efficacy of a behavioral stress reduction group in gay men (39). Compared to a wait-list control, no intervention-related changes in CD4+ cells, NK cells, or PHA lymphocyte responses were observed during the intervention. Mood effects were not examined (39). Overall, findings suggest that immunologic effects are unlikely if interventions fail to improve psychological adjustment.

Managing the Emerging Symptoms of HIV Infection

The onset of symptoms of HIV infection can result in increased anxiety and depression as well as a resurgence of traumatic ideation from diagnosis. Psychological interventions may provide an opportunity for individuals to acquire new skills for coping with the emergence of symptoms. In one RCT, mildly symptomatic gay men who were randomized to CBSM or a modified wait-list control condition (34,42,49). Men in the modified wait-list control were invited to attend a 1-day seminar after the 10-week intervention period. Findings indicated that men in CBSM reported decreases in depressive symptoms, anxiety, and mood disturbance as well as increases in cognitive coping and perceived social support during the intervention. Effects of CBSM on the use of adaptive cognitive coping strategies (acceptance and positive reframing) and perceived social support mediated reductions in distress during the 10 weeks (34). Increases in the use of positive reframing during CBSM also mediated reductions in depressive symptoms over a 6-month follow-up (40). The psychoneuroimmunologic framework underlying the RCTs of CBSM proposes that mood improvements are related to potentially immunomodulatory hormonal changes (12). This appeared to be the case with men in these CBSM groups showing decreases in 24-hour cortisol and norepinephrine (NE), reductions in the plasma cortisol/dehydroepiandrosterone-sulfate (DHEA-S) ratio, and increased plasma testosterone (49-53). Reductions in NE paralleled decreases in anxiety (49). Decreases in urinary cortisol and plasma cortisol/DHEA-S as well as increased plasma testosterone paralleled decreases in depressed mood (51-54).

Men randomized to CBSM also displayed improved anti-viral and cellular immunity compared to those in the modified wait-list control (42,54,55). CBSM decreased herpes simplex virus type 2 (HSV-2; genital herpes) IgG titers during the intervention and buffered against increases in EBV IgG titers through a 6-12 month follow-up. The effect of CBSM on HSV-2 IgG titers was partially mediated by reductions in depressive symptoms as well as increases in social support (42,54), while CBSM effects on EBV IgG titers paralleled sustained increases in social support (55). CBSM also buffered against declines in cytotoxic-suppressor (CD8+) T-cells at 1-year follow-up, and this was mediated by greater reductions in NE during the intervention (50). Finally, men in CBSM displayed increases in transitional naïve T-cells through 1-year follow-up (56), an effect mediated by decreases in depressive symptoms and 24-hour cortisol during the intervention (54). Although findings from these studies were based on different cohorts of men in this RCT, tests of mediation generally indicate that improvements in psychological adjustment are a key determinant of intervention effects on neuroendocrine hormone regulation and immune status.

Coming to Terms with AIDS

Even in the HAART era, individuals living with AIDS grapple with existential challenges related to declines in functional status and health-related quality of life as well as the ever present threat of mortality (57,58). One trial examined the efficacy of a CBSM intervention that included components of supportive/expressive therapy (SET) to promote the expression of negative emotions and detoxify issues related to death and dying in women with AIDS (59). Compared to an attention-matched control that watched educational videotapes, no effects of CBSM+SET were observed on CD4+ cell counts or HIV viral load during the 10-week intervention. CBSM+SET effects on psychological adjustment were not examined, but increases in self-efficacy during the intervention period were associated with concurrent increases in CD4+ counts and declines in HIV viral load.

Bereavement interventions assist HIV-positive individuals with managing grief and distress associated with the loss of a loved one to AIDS. Goodkin and colleagues observed that a group-based bereavement intervention for HIV-positive and HIV-negative gay men was efficacious in reducing grief and distress during the 10-week intervention period compared to a community referral condition (45). HIV-positive men in the bereavement intervention displayed reductions in plasma cortisol and reported fewer health care visits through a 6-month follow-up (60). Significant intervention effects were reported for CD4+ counts over the same period. However, among the sub-sample of HIV-positive men, there were no intervention effects on CD4+ counts at follow-up. Interestingly, higher plasma cortisol was associated with lower CD4+ cell counts among HIV-positive men. There were no concurrent intervention effects on the ratio of CD4 + to CD8+ cells (CD4:CD8). Other findings indicated that control participants displayed increases in HIV viral load during the intervention while men in the bereavement intervention showed no change (61). Although interventions appear to assist HIV-positive individuals in coping with bereavement, Sikkema and colleagues have observed that women and individuals who are at risk for a complicated bereavement appear to derive the most psychological benefit (62,63). Future RCTs should examine the efficacy of bereavement interventions in these populations.

Managing HAART Regimens

HAART is a demanding, unforgiving treatment regimen that requires unprecedented levels of patient adherence to maximize the clinical benefits (64,65). Interventions that focus exclusively on enhancing HAART adherence have been shown to be efficacious (66). Two RCTs examined whether including cognitive-behavioral interventions to improve psychological adjustment enhances the long-term efficacy of HAART adherence interventions as reflected in control of viral load (38,43,67,68). Antoni and colleagues sought to determine whether there was any added benefit to providing CBSM in combination with medication adherence training (MAT) compared to MAT alone in a sample of HAART-treated gay men (43,67). CBSM+MAT decreased depressed mood and denial coping over the 10-week intervention but there were no effects on self-reported adherence. No intervention effects on immune status were observed in intent-to-treat analyses. However, in a sub-sample of the men who had detectable viral load at baseline (n =101), those in CBSM+MAT displayed a statistically significant and clinically important decrease in HIV viral load (.56 $\log_{10}$) through 15 months post-randomization. Reductions in depressed mood during the intervention mediated the sustained effect of CBSM +MAT on HIV viral load after controlling for self-reported HAART adherence. Lending support to these findings, Safren and colleagues examined the efficacy of a 12-week individual cognitive-behavioral intervention for adherence and depression in depressed men and women. Over the intervention period, individuals in the cognitive-behavioral treatment reported reductions in depressive symptoms and displayed increases in electronically monitored HAART adherence compared to those who received a single session adherence intervention (38). Participants in the cognitive-behavioral intervention also displayed decreases in HIV viral

load through 9-month follow-up, but due to the cross-over trial design there was no comparison condition (38). Taken together, these RCTs support the efficacy of cognitive-behavioral treatments in combination with problem-focused HAART adherence interventions.

Is Interpersonal Therapy Superior to Cognitive-Behavioral Therapy?

One RCT examined the efficacy of four individual interventions with depressed men and women who were at various stages of HIV infection (46). Individuals randomized to interpersonal therapy and supportive therapy with imipramine displayed greater reductions in depressive symptoms and increases in physical functioning over the 16-week intervention period compared to either cognitive-behavioral therapy or supportive therapy alone. However, no group differences in CD4+ count were observed over the 16 weeks. Because the association between distress and cellular immunity is most reliably observed in individuals with low viral burden (69), the fact that a substantial minority of participants in this pre-HAART era RCT were at advanced stages of HIV disease may have obscured any effects on immune status. The small sample in each treatment arm and the lack of long-term follow-up also make interpretation of negative effects for CD4+ count difficult. RCTs are needed to examine the differential efficacy of interpersonal and cognitive-behavioral approaches in HAART-treated persons, especially those who present with clinical depression.

Relaxation Training and Meditation-Based Interventions

Relaxation training and meditation-based interventions may improve psychological adjustment, decrease physiologic arousal, and enhance immune status among HIV-positive persons (70-75). One RCT observed that asymptomatic gay men in a 10-week relaxation training program (progressive muscle relaxation, biofeedback, meditation, and hypnosis) reported reductions in distress and anxiety during the intervention compared to an assessment only control (70). Intervention effects on distress paralleled concurrent increases in CD4+ counts, but no group differences were observed at post-intervention. In another small RCT, Auerbach and colleagues determined that symptomatic gay men in an 8-week relaxation training group (thermal biofeedback, guided imagery, and hypnosis) reported increases in vigor and hardiness as well as decreases in HIV-related symptoms during the intervention compared to a wait-list control (71). No concurrent effects on negative affect or CD4+ counts were observed over this short follow-up period (71).

Relatively little is known about the differential efficacy of distinct forms of relaxation training or meditation. One RCT examined 6-week progressive muscle relaxation or guided imagery interventions delivered to men and women via audiotape after brief face-to-face instruction (72). Compared to an assessment only condition, progressive muscle relaxation reduced depressive symptoms and increased CD4+ counts while guided imagery decreased fatigue (an important HIV-related symptom) during the intervention (72). Diego and colleagues also examined the efficacy of a 12-week progressive muscle relaxation intervention compared to a 12-week massage therapy intervention in adolescents (75). Both treatments were delivered twice a week in 20-minute sessions. Participants in both conditions reported reductions in anxiety, but only the massage therapy group reported reductions in depressive symptoms during the intervention. Decreases in depressive symptoms were paralleled by concurrent increases in NK counts, NKCC, CD4+ counts, and CD4:CD8 in the massage therapy group only. Results support the efficacy of massage therapy, but progressive muscle relaxation may not have been delivered with the frequency necessary to reduce depressive symptoms (72). Although further research is necessary to examine the efficacy of distinct forms of relaxation training or meditation, findings from these small RCTs indicate that interventions that successfully reduce depressive symptoms appear to be more likely to enhance immune status. RCTs of mindfulness-based stress reduction are currently being conducted and these may

provide further data regarding the efficacy of relaxation and meditation interventions with HIV-positive persons.

Written Emotional Expression Interventions

Investigations with healthy populations support the efficacy of writing about stress and trauma (written emotional expression) for improving psychological adjustment and immune status (76). Written emotional expression provides an opportunity for individuals to confront traumatic experiences and it may create positive outcome expectancies for emotion regulation (77,78). In a small HAART era RCT, HIV-positive men and women were randomized to 4 sessions of writing about their worst stressful event or writing about trivial daily events (79). Those writing about their worst stressor had reduced HIV viral load at 2 weeks post-randomization and increased CD4+ counts over a 6-month follow-up compared to the trivial writing control. More definitive RCTs of written emotional expression are needed to replicate these findings.

Summary

Of the 14 RCTs that were examined in this review, seven observed intervention effects on HIV disease markers. Consistent with RCTs examining whether psychotherapy prolongs survival in patients with various types of cancer (80), interventions that do not successfully improve psychological adjustment may be less likely to enhance immune status among HIV-positive persons. In fact, three of the seven RCTs that reported negative findings for immune status either did not examine or found no evidence indicating intervention effects on any indicator of psychological adjustment (39,44,59). Although two of the RCTs with negative findings did observe improvements in some indicators of psychological adjustment, these interventions did not reduce depressive symptoms (71,75). Depressive symptoms have been linked to more rapid HIV disease progression across a number of studies (4), but it would be premature to state that reductions in depressive symptoms are necessary for psychological interventions to influence HIV disease markers. Of the two remaining RCTs with negative findings, one compared two interventions that were equally efficacious in reducing depressive symptoms with a small sample that was not powered to detect differences in immune status between two active treatments (33,48). The last RCT where null findings were reported was conducted in the pre-HAART era (46), and the fact that a substantial minority of participants were at advanced stages of HIV disease may have obscured any intervention effects on immune status. This highlights that improvements in psychological adjustment may be necessary but not sufficient for interventions to have salutary effects on immune status. Future RCTs should closely attend to inclusion criteria in order to enroll cohorts that are more likely to display changes in HIV disease markers that may be linked to intervention-related effects on psychological adjustment (67).

Although it appears that psychological intervention effects on immune status were more reliably observed among individuals at the earlier stages of HIV infection, only one published RCT has examined the efficacy of an intervention for individuals living with AIDS (59), thereby making comparisons by disease-stage hazardous. While individuals may meet criteria for AIDS based on medical history, substantial improvements in immune status among those taking HAART may increase the responsiveness of the immune system to changes in psychological adjustment. Interestingly, two of the three RCTs conducted in the HAART era reported that psychological interventions enhanced immune status in samples that were diverse with respect to HIV disease stage (67,75,79), but conclusions based on such as small number of trials would be premature. Because HIV-positive persons continue to endure a chronic, unpredictable disease with increased burdens related to managing HAART regimens,

psychological interventions represent a viable adjuvant treatment that can assist patients with improving psychological adjustment and potentially enhancing immune status.

Limitations and Directions for Future Research

There are numerous methodological limitations of the RCTs reviewed above. The major limitation is the lack of clarity regarding the active element(s) of these multi-modal interventions. For example, in two RCTs of CBSM greater home relaxation practice was associated with mood improvements, increases in immune parameters, and decreases in salivary cortisol (42,81,82). While these findings are provocative, it is difficult to determine whether they support the efficacy of the relaxation training component of CBSM or if they are a marker for better adherence to the overall intervention protocol. Deconstruction trials are necessary to examine the efficacy of distinct components of psychological interventions in comparison to non-specific social support effects. The vast majority of RCTs did not include attention-matched control conditions. Without an attention-matched control, it is difficult to determine whether the effects are specific to these interventions or non-specific effects of any psychological treatment. Bearing in mind that the magnitude of intervention effects on psychological adjustment is variable across the six RCTs included in this review that provided sufficient descriptive data to calculate an effect size statistic (Cohen's d Range = .11 to .54; Median = .31), deconstruction trials may inform the development of innovative interventions for HIV-positive persons with potentially superior efficacy. Deconstruction trials should also specifically examine what aspects of stress and coping interventions cultivate positive psychological states (11,83-86), and if components of these treatments that modify positive psychological states influence HIV disease markers.

Future efficacy trials of psychological interventions for HIV-positive persons should also attempt to improve upon the numerous methodological limitations that are evident in RCTs that have been conducted to date. Most trials examined the effects of psychological interventions with small samples and it is possible that many did not have the power necessary to detect effects on immune status. However, effect size estimates for the six RCTs that included sufficient descriptive data to compute this statistic generally indicated a lack of intervention effects on CD4+ counts (Cohen's d range = -.77 to .31; Median = -.17). Because of the heterogeneity of other HIV disease markers examined, it was not possible to calculate reliable estimates for the effect size range. It is noteworthy that only six trials have examined the sustained effects (beyond the immediate post-intervention assessment) of psychological interventions on measures of immune status. Changes in immune status may emerge over longer periods and future RCTs with sufficient power should include long-term follow-up assessments to conduct more definitive tests of intervention effects on HIV disease markers. This is supported by findings from a RCT of CBSM+MAT where clinically important reductions in HIV viral load emerged over a long-term follow-up (67). Including follow-up assessments will also be crucial to examine the effects of psychological interventions on clinically relevant outcomes such as progression to AIDS and mortality. While enhanced immunosurveillance may have implications for protection against future development of opportunistic infections and neoplasias (12), no investigation to date has reported intervention effects on clinically relevant outcomes. An important first step may be examining well-defined pathophysiological pathways such as progression of virally-initiated neoplasias, which has been associated with elevated life stress (87).

It is also noteworthy that the majority of RCTs examining the effects psychological interventions have been well-controlled efficacy trials with extensive exclusion criteria that were conducted mostly with gay men. While there is some support for the efficacy of cognitive-behavioral interventions with HIV-positive women (88,89) and heterosexual men (32), it is worth examining whether treatments that intervene at the family level will demonstrate superior

efficacy for these groups (90-92). It is clear that there is a need for more trials examining the efficacy of psychological interventions for women and heterosexual men living with HIV/AIDS. In addition, the stringent inclusion criteria of well-controlled efficacy trials limit the external validity of intervention effects that have been observed. Despite the fact that a substantial minority of HIV-positive persons have co-morbid substance use disorders (93), these individuals have commonly been excluded from previous efficacy trials of psychological interventions. Future investigations should develop and test innovative psychological interventions that are designed to meet the unique needs of substance users. In particular, individuals who regularly use stimulants such as cocaine and methamphetamine may be good candidates for psychological interventions because they are more likely to be non-adherent to HAART and display poor suppression of HIV viral load (94,95).

Finally, despite the past 20 years of research to develop and test the efficacy of innovative psychological interventions for HIV-positive persons, there is insufficient data regarding the clinical relevance and policy implications. It is unclear to what extent these treatments are being implemented in the context of regular medical care or at community-based organizations. Another important, unanswered question is whether psychological interventions can be tailored to meet the needs of individuals living with HIV/AIDS in the developing world to improve psychological adjustment and immune status. Effectiveness trials of promising psychological interventions with more representative samples of HIV-positive persons in varied settings are needed to provide more definitive information on the clinical utility of these treatments and their potential cost-effectiveness.

Acknowledgements

This review was supported in part by National Institute of Mental Health Grants T32 MH019391 (PI: Nancy Adler, Ph.D.) and T32 MH18917 (PI: Neil Schneiderman, Ph.D.).

References

1. Whetten, K. Psychosomatic Medicine HIV/AIDS Supplement Article.
2. Heckman TG, Anderson ES, Sikkema KJ, Kochman A, Kalichman SC, Anderson T. Emotional distress in nonmetropolitan persons living with HIV disease enrolled in a telephone-delivered, coping improvement group intervention. Health Psychol 2004;23:94–100. [PubMed: 14756608]
3. Weaver KE, Llabre MM, Duran RE, Antoni MH, Ironson G, Penedo FJ, Schneiderman N. A stress and coping model of medication adherence and viral load in HIV-positive men and women on highly active antiretroviral therapy (HAART). Health Psychol 2005;24:385–92. [PubMed: 16045374]
4. Leserman, J. Psychosomatic Medicine HIV/AIDS Supplement Article.
5. Moskowitz JT. Positive affect predicts lower risk of AIDS mortality. Psychosom Med 2003;65:620–6. [PubMed: 12883113]
6. Carrico AW, Ironson G, Antoni MH, Lechner SC, Duran RE, Kumar M, Schneiderman N. A path model of the effects of spirituality on depressive symptoms and 24-h urinary-free cortisol in HIV-positive persons. J Psychosom Res 2006;61:51–8. [PubMed: 16813845]
7. Ickovics JR, Milan S, Boland R, Schoenbaum E, Schuman P, Vlahov D. Psychological resources protect health: 5-year survival and immune function among HIV-infected women from four US cities. Aids 2006;20:1851–60. [PubMed: 16954726]
8. Gonzalez JS, Penedo FJ, Antoni MH, Duran RE, McPherson-Baker S, Ironson G, Isabel Fernandez M, Klimas NG, Fletcher MA, Schneiderman N. Social support, positive states of mind, and HIV treatment adherence in men and women living with HIV/AIDS. Health Psychol 2004;23:413–8. [PubMed: 15264978]
9. Moskowitz JT, Folkman S, Acree M. Do positive psychological states shed light on recovery from bereavement? Findings from a 3-year longitudinal study. Death Stud 2003;27:471–500. [PubMed: 12814129]
10. Ironson, G. Psychosomatic Medicine HIV/AIDS Supplement Article.

11. Chesney MA, Darbes LA, Hoerster K, Taylor JM, Chambers DB, Anderson DE. Positive emotions: exploring the other hemisphere in behavioral medicine. Int J Behav Med 2005;12:50–8. [PubMed: 15901213]
12. Antoni MH. Stress management and psychoneuroimmunology in HIV infection. CNS Spectr 2003;8:40–51. [PubMed: 12627048]
13. Miller GE, Cohen S. Psychological interventions and the immune system: a meta-analytic review and critique. Health Psychol 2001;20:47–63. [PubMed: 11199066]
14. Dybul M, Fauci AS, Bartlett JG, Kaplan JE, Pau AK. Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. Ann Intern Med 2002;137:381–433. [PubMed: 12617573]
15. Klimas NG, Caralis P, LaPerriere A, Antoni MH, Ironson G, Simoneau J, Schneiderman N, Fletcher MA. Immunologic function in a cohort of human immunodeficiency virus type 1-seropositive and -negative healthy homosexual men. J Clin Microbiol 1991;29:1413–21. [PubMed: 1885736]
16. Ironson G, Balbin E, Solomon G, Fahey J, Klimas N, Schneiderman N, Fletcher MA. Relative preservation of natural killer cell cytotoxicity and number in healthy AIDS patients with low CD4 cell counts. AIDS 2001;15:2065–73. [PubMed: 11684925]
17. Laurence J. Molecular interactions among herpesviruses and human immunodeficiency viruses. J Infect Dis 1990;162:338–46. [PubMed: 2165107]
18. Montagnier L, Gruest J, Chamaret S, Dauguet C, Axler C, Guetard D, Nugeyre MT, Barre-Sinoussi F, Chermann JC, Brunet JB, et al. Adaptation of lymphadenopathy associated virus (LAV) to replication in EBV-transformed B lymphoblastoid cell lines. Science 1984;225:63–6. [PubMed: 6328661]
19. McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998;338:171–9. [PubMed: 9428819]
20. Cole, SW. Psychosomatic Medicine HIV/AIDS Supplement Article.
21. Markham PD, Salahuddin SZ, Veren K, Orndorff S, Gallo RC. Hydrocortisone and some other hormones enhance the expression of HTLV-III. Int J Cancer 1986;37:67–72. [PubMed: 3000956]
22. Norbiato G, Bevilacqua M, Vago T, Taddei A, Clerici. Glucocorticoids and the immune function in the human immunodeficiency virus infection: a study in hypercortisolemic and cortisol-resistant patients. J Clin Endocrinol Metab 1997;82:3260–3. [PubMed: 9329349]
23. Nair MPN, Mahajan S, Hou J, Sweet AM, Schwartz SA. The stress hormone, cortisol, synergizes with HIV-1 gp-120 to induce apoptosis of normal human periperhial blood mononuclear cells. Cell Mol Biol 2000;46:1227–38. [PubMed: 11075952]
24. Gougeon ML. Programmed cell death in HIV infection: dysregulation of BCL-2 and Fas pathways and contribution to AIDS pathogenesis. Psychoneuroendocrinology 1997;22(Suppl 1):S33–9. [PubMed: 9264145]
25. Leserman J, Petitto JM, Gu H, Gaynes BN, Barroso J, Golden RN, Perkins DO, Folds JD, Evans DL. Progression to AIDS, a clinical AIDS condition and mortality: psychosocial and physiological predictors. Psychol Med 2002;32:1059–73. [PubMed: 12214787]
26. Cole SW, Korin YD, Fahey JL, Zack JA. Norepinephrine accelerates HIV replication via protein kinase A-dependent effects on cytokine production. J Immunol 1998;161:610–6. [PubMed: 9670934]
27. Cole SW, Naliboff BD, Kemeny ME, Griswold MP, Fahey JL, Zack JA. Impaired response to HAART in HIV-infected individuals with high autonomic nervous system activity. Proc Natl Acad Sci U S A 2001;98:12695–700. [PubMed: 11675501]
28. Beck, J. Cognitive Therapy: Basics and Beyond. Guilford Press; New York: 1995.
29. Antoni, MH. Behavioural interventions and psychoneuroimmunology. In: Vedhara, K.; Irwin, M., editors. Human Psychoneuroimmunology. Oxford University Press; Oxford: 2005. p. 283-318.
30. Antoni, M.; Ironson, G.; Schneiderman, N. Cognitive Behavioral Stress Management for Individuals Living with HIV: Facilitator Guide. Oxford University Press; Oxford: 2007.
31. Antoni, M.; Ironson, G.; Schneiderman, N. Cognitive Behavioral Stress Management: Workbook. Oxford University Press; Oxford: 2007.
32. Chan I, Kong P, Leung P, Au A, Li P, Chung R, Po LM, Yu P. Cognitive-behavioral group program for Chinese heterosexual HIV-infected men in Hong Kong. Patient Educ Couns 2005;56:78–84. [PubMed: 15590226]

33. Mulder CL, Emmelkamp PM, Antoni MH, Mulder JW, Sandfort TG, de Vries MJ. Cognitive-behavioral and experiential group psychotherapy for HIV-infected homosexual men: a comparative study. Psychosom Med 1994;56:423–31. [PubMed: 7809342]
34. Lutgendorf SK, Antoni MH, Ironson G, Starr K, Costello N, Zuckerman M, Klimas N, Fletcher MA, Schneiderman N. Changes in cognitive coping skills and social support during cognitive behavioral stress management intervention and distress outcomes in symptomatic human immunodeficiency virus (HIV)-seropositive gay men. Psychosom Med 1998;60:204–14. [PubMed: 9560871]
35. Kelly JA, Murphy DA, Bahr GR, Kalichman SC, Morgan MG, Stevenson LY, Koob JJ, Brasfield TL, Bernstein BM. Outcome of cognitive-behavioral and support group brief therapies for depressed, HIV-infected persons. Am J Psychiatry 1993;150:1679–86. [PubMed: 8214177]
36. O'Leary A, Hoff CC, Purcell DW, Gomez CA, Parsons JT, Hardnett F, Lyles CM. What happened in the SUMIT trial? Mediation and behavior change. Aids 2005;19(Suppl 1):S111–21. [PubMed: 15838189]
37. Rotheram-Borus M, Murphy DA, Wight RG, Lee MB, Lightfoot M, Swendeman D, Birnbaum JM, Wright W. Improving quality of life among young people living with HIV. Evaluation and Program Planning 2001;24:227–237.
38. Safren S, O'Cleirigh C, Tan J, Raminani S, Reilly L, Otto MW, Mayer KH. Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. Under Review.
39. Coates TJ, McKusick L, Kuno R, Stites DP. Stress reduction training changed number of sexual partners but not immune function in men with HIV. Am J Public Health 1989;79:885–7. [PubMed: 2735479]
40. Carrico AW, Antoni MH, Weaver KE, Lechner SC, Schneiderman N. Cognitive-behavioural stress management with HIV-positive homosexual men: mechanisms of sustained reductions in depressive symptoms. Chronic Illn 2005;1:207–15. [PubMed: 17152183]
41. Antoni MH, Baggett L, Ironson G, LaPerriere A, August S, Klimas N, Schneiderman N, Fletcher MA. Cognitive-behavioral stress management intervention buffers distress responses and immunologic changes following notification of HIV-1 seropositivity. J Consult Clin Psychol 1991;59:906–15. [PubMed: 1774375]
42. Lutgendorf SK, Antoni MH, Ironson G, Klimas N, Kumar M, Starr K, McCabe P, Cleven K, Fletcher MA, Schneiderman N. Cognitive-behavioral stress management decreases dysphoric mood and herpes simplex virus-type 2 antibody titers in symptomatic HIV-seropositive gay men. J Consult Clin Psychol 1997;65:31–43. [PubMed: 9103732]
43. Carrico AW, Antoni MH, Duran RE, Ironson G, Penedo F, Fletcher MA, Klimas N, Schneiderman N. Reductions in depressed mood and denial coping during cognitive behavioral stress management with HIV-Positive gay men treated with HAART. Ann Behav Med 2006;31:155–64. [PubMed: 16542130]
44. Cleary PD, Van Devanter N, Steilen M, Stuart A, Shipton-Levy R, McMullen W, Rogers TF, Singer E, Avorn J, Pindyck J. A randomized trial of an education and support program for HIV-infected individuals. AIDS 1995;9:1271–8. [PubMed: 8561981]
45. Goodkin K, Blaney NT, Feaster DJ, Baldewicz T, Burkhalter JE, Leeds B. A randomized controlled clinical trial of a bereavement support group intervention in human immunodeficiency virus type 1-seropositive and -seronegative homosexual men. Arch Gen Psychiatry 1999;56:52–9. [PubMed: 9892256]
46. Markowitz JC, Kocsis JH, Fishman B, Spielman LA, Jacobsberg LB, Frances AJ, Klerman GL, Perry SW. Treatment of depressive symptoms in human immunodeficiency virus-positive patients. Arch Gen Psychiatry 1998;55:452–7. [PubMed: 9596048]
47. LaPerriere AR, Antoni MH, Schneiderman N, Ironson G, Klimas N, Caralis P, Fletcher MA. Exercise intervention attenuates emotional distress and natural killer cell decrements following notification of positive serologic status for HIV-1. Biofeedback Self Regul 1990;15:229–42. [PubMed: 2223891]
48. Mulder CL, Antoni MH, Emmelkamp PM, Veugelers PJ, Sandfort TG, van de Vijver FA, de Vries MJ. Psychosocial group intervention and the rate of decline of immunological parameters in asymptomatic HIV-infected homosexual men. Psychother Psychosom 1995;63:185–92. [PubMed: 7624465]

49. Antoni MH, Cruess DG, Cruess S, Lutgendorf S, Kumar M, Ironson G, Klimas N, Fletcher MA, Schneiderman N. Cognitive-behavioral stress management intervention effects on anxiety, 24-hr urinary norepinephrine output, and T-cytotoxic/suppressor cells over time among symptomatic HIV-infected gay men. J Consult Clin Psychol 2000;68:31–45. [PubMed: 10710838]
50. Antoni MH, Cruess S, Cruess DG, Kumar M, Lutgendorf S, Ironson G, Dettmer E, Williams J, Klimas N, Fletcher MA, Schneiderman N. Cognitive-behavioral stress management reduces distress and 24-hour urinary free cortisol output among symptomatic HIV-infected gay men. Ann Behav Med 2000;22:29–37. [PubMed: 10892526]
51. Cruess DG, Antoni MH, Schneiderman N, Ironson G, McCabe P, Fernandez JB, Cruess SE, Klimas N, Kumar M. Cognitive-behavioral stress management increases free testosterone and decreases psychological distress in HIV-seropositive men. Health Psychol 2000;19:12–20. [PubMed: 10711583]
52. Cruess DG, Antoni MH, Kumar M, Ironson G, McCabe P, Fernandez JB, Fletcher M, Schneiderman N. Cognitive-behavioral stress management buffers decreases in dehydroepiandrosterone sulfate (DHEA-S) and increases in the cortisol/DHEA-S ratio and reduces mood disturbance and perceived stress among HIV-seropositive men. Psychoneuroendocrinology 1999;24:537–49. [PubMed: 10378240]
53. Antoni MH, Cruess DG, Klimas N, Carrico AW, Maher K, Cruess S, Lechner SC, Kumar M, Lutgendorf S, Ironson G, Fletcher MA, Schneiderman N. Increases in a marker of immune system reconstitution are predated by decreases in 24-h urinary cortisol output and depressed mood during a 10-week stress management intervention in symptomatic HIV-infected men. J Psychosom Res 2005;58:3–13. [PubMed: 15771864]
54. Cruess S, Antoni M, Cruess D, Fletcher MA, Ironson G, Kumar M, Lutgendorf S, Hayes A, Klimas N, Schneiderman N. Reductions in herpes simplex virus type 2 antibody titers after cognitive behavioral stress management and relationships with neuroendocrine function, relaxation skills, and social support in HIV-positive men. Psychosom Med 2000;62:828–37. [PubMed: 11139003]
55. Carrico AW, Antoni MH, Pereira DB, Fletcher MA, Klimas N, Lechner SC, Schneiderman N. Cognitive behavioral stress management effects on mood, social support, and a marker of antiviral immunity are maintained up to 1 year in HIV-infected gay men. Int J Behav Med 2005;12:218–26. [PubMed: 16262540]
56. Antoni MH, Cruess DG, Klimas N, Maher K, Cruess S, Kumar M, Lutgendorf S, Ironson G, Schneiderman N, Fletcher MA. Stress management and immune system reconstitution in symptomatic HIV-infected gay men over time: effects on transitional naive T cells (CD4(+)CD45RA(+)CD29(+)). Am J Psychiatry 2002;159:143–5. [PubMed: 11772706]
57. Liu C, Johnson L, Ostrow D, Silvestre A, Visscher B, Jacobson LP. Predictors for lower quality of life in the HAART era among HIV-infected men. J Acquir Immune Defic Syndr 2006;42:470–7. [PubMed: 16810114]
58. Martinez E, Milinkovic A, Buira E, de Lazzari E, Leon A, Larrousse M, Lonca M, Laguno M, Blanco J, Mallolas J, Garcia F, Miro J, Gatell J. Incidence and causes of death in HIV-infected persons receiving highly active antiretroviral therapy compared with estimates for the general population of similar age and from the same geographical area. HIV Med 2007;8:251–8. [PubMed: 17461853]
59. Ironson G, Weiss S, Lydston D, Ishii M, Jones D, Asthana D, Tobin J, Lechner S, Laperriere A, Schneiderman N, Antoni M. The impact of improved self-efficacy on HIV viral load and distress in culturally diverse women living with AIDS: The SMART/EST Women's Project. AIDS Care 2007;17:222–236. [PubMed: 15763716]
60. Goodkin K, Feaster DJ, Asthana D, Blaney NT, Kumar M, Baldewicz T, Tuttle RS, Maher KJ, Baum MK, Shapshak P, Fletcher MA. A bereavement support group intervention is longitudinally associated with salutary effects on the CD4 cell count and number of physician visits. Clin Diagn Lab Immunol 1998;5:382–91. [PubMed: 9605995]
61. Goodkin K, Baldewicz TT, Asthana D, Khamis I, Blaney NT, Kumar M, Burkhalter JE, Leeds B, Shapshak P. A bereavement support group intervention affects plasma burden of human immunodeficiency virus type 1. Report of a randomized controlled trial. J Hum Virol 2001;4:44–54. [PubMed: 11213933]

62. Sikkema KJ, Hansen NB, Kochman A, Tate DC, Difranceisco W. Outcomes from a randomized controlled trial of a group intervention for HIV positive men and women coping with AIDS-related loss and bereavement. Death Stud 2004;28:187–209. [PubMed: 15053030]
63. Sikkema KJ, Hansen NB, Ghebremichael M, Kochman A, Tarakeshwar N, Meade CS, Zhang H. A randomized controlled trial of a coping group intervention for adults with HIV who are AIDS bereaved: longitudinal effects on grief. Health Psychol 2006;25:563–70. [PubMed: 17014273]
64. Bangsberg DR, Acosta EP, Gupta R, Guzman D, Riley ED, Harrigan PR, Parkin N, Deeks SG. Adherence-resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virological fitness. AIDS 2006;20:223–31. [PubMed: 16511415]
65. Johnson MO, Catz SL, Remien RH, Rotheram-Borus MJ, Morin SF, Charlebois E, Gore-Felton C, Goldsten RB, Wolfe H, Lightfoot M, Chesney MA. Theory-guided, empirically supported avenues for intervention on HIV medication nonadherence: findings from the Healthy Living Project. AIDS Patient Care STDS 2003;17:645–56. [PubMed: 14746658]
66. Simoni JM, Frick PA, Pantalone DW, Turner BJ. Antiretroviral adherence interventions: a review of current literature and ongoing studies. Top HIV Med 2003;11:185–98. [PubMed: 14724327]
67. Antoni MH, Carrico AW, Duran RE, Spitzer S, Penedo F, Ironson G, Fletcher MA, Klimas N, Schneiderman N. Randomized clinical trial of cognitive behavioral stress management on human immunodeficiency virus viral load in gay men treated with highly active antiretroviral therapy. Psychosom Med 2006;68:143–51. [PubMed: 16449425]
68. Safren S, Knauz RO, O'Cleirigh C, Lerner J, Greer J, Harwood M, Tan J, Mayer KH. CBT for HIV medication adherence and depression: Process and outcome at post-treatment and three-month cross over. Ann Behav Med 2006;31:S006.
69. Motivala SJ, Hurwitz BE, Llabre MM, Klimas NG, Fletcher MA, Antoni MH, LeBlanc WG, Schneiderman N. Psychological distress is associated with decreased memory helper T-cell and B-cell counts in pre-AIDS HIV seropositive men and women but only in those with low viral load. Psychosom Med 2003;65:627–35. [PubMed: 12883114]
70. Taylor DN. Effects of a behavioral stress-management program on anxiety, mood, self-esteem, and T-cell count in HIV positive men. Psychol Rep 1995;76:451–7. [PubMed: 7667456]
71. Auerbach J, Oleson TD, Solomon GF. A behavioral medicine interventioin as an adjunctive treatment for HIV-related illness. Psychology and Health 1992;6:325–334.
72. Eller L. Effects of two cognitive-behavioral interventions on immunity and symptoms in persons with HIV. Ann Behav Med 1995;17:339–348.
73. Bormann JE, Gifford AL, Shively M, Smith TL, Redwine L, Kelly A, Becker S, Gershwin M, Bone P, Belding W. Effects of spiritual mantram repetition on HIV outcomes: a randomized controlled trial. J Behav Med 2006;29:359–76. [PubMed: 16847590]
74. Bormann J, Carrico AW. Increases in positive reappraisal coping during a group-based mantram intervention mediate sustained reductions in anger in HIV-positive persons. Under Review.
75. Diego MA, Field T, Hernandez-Reif M, Shaw K, Friedman L, Ironson G. HIV adolescents show improved immune function following massage therapy. Int J Neurosci 2001;106:35–45. [PubMed: 11264907]
76. Smyth JM. Written emotional expression: effect sizes, outcome types, and moderating variables. J Consult Clin Psychol 1998;66:174–84. [PubMed: 9489272]
77. Pennebaker JW, Seagal JD. Forming a story: the health benefits of narrative. J Clin Psychol 1999;55:1243–54. [PubMed: 11045774]
78. Langens TA, Schuler J. Effects of written emotional expression: the role of positive expectancies. Health Psychol 2007;26:174–82. [PubMed: 17385969]
79. Petrie KJ, Fontanilla I, Thomas MG, Booth RJ, Pennebaker JW. Effect of written emotional expression on immune function in patients with human immunodeficiency virus infection: a randomized trial. Psychosom Med 2004;66:272–5. [PubMed: 15039514]
80. Spiegel D. Mind matters -- group therapy and survival in breast cancer. N Engl J Med 2001;345:1767–8. [PubMed: 11742052]
81. Cruess DG, Antoni MH, Kumar M, Schneiderman N. Reductions in salivary cortisol are associated with mood improvement during relaxation training among HIV-seropositive men. J Behav Med 2000;23:107–22. [PubMed: 10833675]

82. Ironson G, Friedman A, Klimas N, Antoni M, Fletcher MA, Laperriere A, Simoneau J, Schneiderman N. Distress, denial, and low adherence to behavioral interventions predict faster disease progression in gay men infected with human immunodeficiency virus. Int J Behav Med 1994;1:90–105. [PubMed: 16250807]

83. Chesney M, Folkman S, Chambers D. Coping effectiveness training for men living with HIV: preliminary findings. Int J STD AIDS 1996;7(Suppl 2):75–82. [PubMed: 8799801]

84. Chesney MA, Chambers DB, Taylor JM, Johnson LM, Folkman S. Coping effectiveness training for men living with HIV: results from a randomized clinical trial testing a group-based intervention. Psychosom Med 2003;65:1038–46. [PubMed: 14645783]

85. Heckman TG, Carlson B. A randomized clinical trial of two telephone-delivered, mental health interventions for HIV-infected persons in rural areas of the United States. AIDS Behav 2007;11:5–14. [PubMed: 16705479]

86. Heckman TG, Barcikowski R, Ogles B, Suhr J, Carlson B, Holroyd K, Garske J. A telephone-delivered coping improvement group intervention for middle-aged and older adults living with HIV/AIDS. Ann Behav Med 2006;32:27–38. [PubMed: 16827627]

87. Pereira DB, Antoni MH, Danielson A, Simon T, Efantis-Potter J, Carver CS, Duran RE, Ironson G, Klimas N, O'Sullivan MJ. Life stress and cervical squamous intraepithelial lesions in women with human papillomavirus and human immunodeficiency virus. Psychosom Med 2003;65:427–34. [PubMed: 12764216]

88. Laperriere A, Ironson GH, Antoni MH, Pomm H, Jones D, Ishii M, Lydston D, Lawrence P, Grossman A, Brondolo E, Cassells A, Tobin JN, Schneiderman N, Weiss SM. Decreased depression up to one year following CBSM+ intervention in depressed women with AIDS: the smart/EST women's project. J Health Psychol 2005;10:223–31. [PubMed: 15723892]

89. West-Edwards C, Pereira D, Greenwood D, Antoni MH, Ironson G, Duran R, Fletcher MA, Schneiderman N. An investigation of the psychological and immune effects of a cognitive behavioral stress management (CBSM) intervention for HIV+ African American women. Ann Behav Med 2001;23:12.

90. Rotheram-Borus MJ, Lee MB, Gwadz M, Draimin B. An intervention for parents with AIDS and their adolescent children. Am J Public Health 2001;91:1294–302. [PubMed: 11499122]

91. Stein MD, Herman DS, Bishop D, Anderson BJ, Trisvan E, Lopez R, Flanigan T, Miller I. A telephone-based intervention for depression in HIV patients: negative results from a randomized clinical trial. AIDS Behav 2007;11:15–23. [PubMed: 16779656]

92. Szapocznik J, Feaster DJ, Mitrani VB, Prado G, Smith L, Robinson-Batista C, Schwartz SJ, Mauer MH, Robbins MS. Structural ecosystems therapy for HIV-seropositive African American women: effects on psychological distress, family hassles, and family support. J Consult Clin Psychol 2004;72:288–303. [PubMed: 15065962]

93. Bing EG, Burnam MA, Longshore D, Fleishman JA, Sherbourne CD, London AS, Turner BJ, Eggan F, Beckman R, Vitiello B, Morton SC, Orlando M, Bozzette SA, Ortiz-Barron L, Shapiro M. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. Arch Gen Psychiatry 2001;58:721–8. [PubMed: 11483137]

94. Ellis RJ, Childers ME, Cherner M, Lazzaretto D, Letendre S, Grant I. Increased human immunodeficiency virus loads in active methamphetamine users are explained by reduced effectiveness of antiretroviral therapy. J Infect Dis 2003;188:1820–6. [PubMed: 14673760]

95. Carrico AW, Johnson MO, Moskowitz JT, Neilands TB, Morin SF, Charlebois ED, Steward WT, Remien RH, Lightfoot MA, Rotheram-Borus MJW, Chesney MA. Affect regulation, stimulant use, and viral load among HIV-positive persons on anti-retroviral therapy. Psychosom Med 2007;69:785–792. [PubMed: 17942835]F. L.

Table 1

Randomized Controlled Trials of Psychological Interventions for HIV-Positive Persons that Examined Neuroendocrine or Immune Outcomes

Intervention Type (Ref)	Sample (Control Condition)	Analyses	Limitations‡	Psychological	Neuroendocrine	Immune or Health Status
Cognitive-Behavioral:						
10-wk CBSM Group (41)	23 gay men (Assessment Only)	Pre to Post	D, E	↓ Depression ↓ Anxiety		Buffered ↓ CD4 and NK ↑ PHA Response
10-wk CBSM Group (34,40,42,49-56)	129 gay men (1-Day Seminar)	Pre to Post & Maintenance	C, D, E	↓ Depression ↓ Depressed Mood ↓ Anxiety ↓ Distress	↓ plasma cortisol/DHEA-S ↓ plasma testosterone ↓ 24-hr urinary cortisol ↓ 24-hr urinary NE	Buffered ↓ CD8+ Buffered ↑ EBV IgG ↓ HSV-2 IgG (X) HSV-1 IgG ↑ Transitional Naïve T (X) CD4+
10-wk CBSM+MAT Group (43,67)	130 gay men† (1-Day Seminar & MAT-Only)	Pre to Post & Maintenance	A, C, E	↓ Depressed Mood (X) Anxiety		↓ HIV Viral Load (X) CD4+
15-wk Group (33,48)	39 gay men (Wait-List Control)	Pre to Post & Maintenance	D, E			
a) Cognitive-Behavioral				↓ Depression ↓ Distress		(X) CD4+ (X) Anti-CD3 Response
b) Supportive-Expressive				↓ Depression ↓ Distress		(X) CD4+ (X) Anti-CD3 Response
6-wk Behavioral Group (44)	200 men and women (Community Referral)	Maintenance	B, E	(X) Depression		(X) CD4+; (X) CD4:CD8
8-wk Stress Reduction Group (39)	64 gay men (Wait-List Control)	Pre to Post	E			(X) CD4+; (X) NK (X) PHA Response
16-wk Individual (46)	101 men and women (Supportive Psychotherapy)	Pre to Post	A			
a) Cognitive-Behavioral				(X) Depression		(X) CD4+
b) Interpersonal				↓ Depression		(X) CD4+ ↑ Physical Functioning
10-wk CBSM+SET Group (59)	56 women (Educational Videotape)	Pre to Post	D			(X) CD4+ (X) HIV Viral Load
10-wk Group (45,60-61)	97 bereaved gay men (Community Referral)	Pre to Post & Maintenance	A, D, E	(X) Depression (X) Anxiety ↓ Distress ↓ Grief	↓ Plasma Cortisol	Buffered ↑ Viral Load Buffered ↓ CD4+ (X) CD4:CD8 ↓ Health Care Visits
Relaxation and Meditation:						
6-wk Relaxation Audiotape (72)	69 men and women (Assessment Only)	Pre to Post	A, D, E			
a) Guided Imagery				(X) Depression		(X) CD4+ ↓ Fatigue
b) PMR				↓ Depression		↑ CD4+

Intervention Type (Ref)	Sample (Control Condition)	Analyses	Limitations‡	Psychological	Neuroendocrine	Immune or Health Status
10-wk Relaxation Training (70)	10 gay men (Assessment Only)	Pre to Post	E	↓ Distress ↓ Anxiety		↑ CD4+
8-wk Relaxation Training (71)	26 gay men (Wait-List Control)	Pre to Post	E	(X) Depression (X) Anxiety ↑ Vigor ↑ Hardiness		(X) CD4+ ↓ HIV Symptoms
12-wk PMR (75)	24 Adolescents† (Massage Therapy)	Pre to Post	A	(X) Depression ↓ Anxiety		(X) CD4+ (X) CD4:CD8 (X) NKCC
Emotional Expression:						
4-day Emotional Expression (79)	37 men and women† (Trivial Writing)	Maintenance	A, D			↓ HIV Viral Load ↑ CD4+

CBSM = Cognitive Behavioral Stress Management; SET = Supportive Expressive Therapy; MAT = Medication Adherence Training; PMR = Progressive Muscle Relaxation; (X) = Null Finding Reported; Buffered = Decrements in the comparison condition but no changes in the intervention condition

‡Methodological Limitations: A) participants enrolled the trial were heterogeneous with respect to HIV disease stage; B) low intervention attendance (average of < 50% of sessions attended); C) low follow-up rates (< 75%); D) did not conduct intent-to-treat analyses for all outcomes examined; and E) did not have an attention-matched control condition

†Trial was conducted after the advent of Highly Active Anti-Retroviral Therapy (HAART)