Title
Relationship Functioning & Immune Health in HIV+ Latinas

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**Relationship Functioning & Immune Health in HIV+ Latinas**

Psychoneuroimmunology (PNI) seeks to explain the associations between negative emotions (e.g. depression), social relationships, sociodemographic variables (e.g. SES, gender, ethnicity), and their effects upon immune regulation, the hypothalamic-pituitary-adrenal axis (HPA) and the sympathetic nervous system (SNS). Gaining a clearer understanding of these intricate interactions is essential for improved prevention and treatment of both psychological and physiological complications that may arise throughout the course of HIV, via both psychotherapeutic and medical interventions. These interactions have been demonstrated in immunological outcomes in cancer, infectious disease, wound healing, autoimmune disease, and HIV (Kiecolt-Glaser et al., 2002) in a variety of populations.

The *stress/social support hypothesis* is essentially a PNI framework for capturing the connections between relationship factors, psychological processes, health-related behavior, and physiological consequences, and how these associations affect health status. Burman and Margolin (1992) theorize that relationship status, quality, and interaction lead to stress or support, which, in turn differentially affects one’s cognitions, affect, and health related behavior. These psychological processes lead to a variety of physiological processes (e.g. arousal, CAD, immune response, virus susceptibility), which ultimately determines one’s overall health status. However, the overall conceptual framework for this hypothesis is quite expansive and all-encompassing, including consideration of interpersonal, personality, and coping variables. Although my upcoming study is based on the hypothesized associations proposed by the stress/social support hypothesis, the scope of my proposed study has been limited to examining only relationship quality and status, depression, and HIV-related immune health variables in Latina women.
Literature linking psychosocial variables to immunological change and disease progression in HIV has grown in the past decade. As there is a considerable amount of variability throughout the course of the disease, which suggests a variety of factors affecting disease progression, studying HIV-infected individuals by means of a PNI framework is promising (Eisenberger, Kemeny & Wyatt, 2003). The immunologic pathways related to HIV are well understood and are easily measured, and a body of research has documented the connections between psychosocial issues and morbidity and mortality in homosexual HIV-seropositive men (Cole, Kemeny, Taylor, Visscher & Fahey, 1996). However, there is a noticeable dearth of studies that have examined these connections among women, and as the course of HIV varies widely between men and women (Kalichman, 1998), previous findings on men cannot be assumed to generalize to women. This lack of research has considerable implications with regards to diagnosis, medical treatment, prevention methods, and understanding psychosocial factors pertinent to women (Carney, 2003). Given the alarming increase in the rate of HIV infections in women of color, it is imperative to include them in PNI research.

Although Latina and African-Americans comprise only 20% of the U.S. population, they account for more than 80% of AIDS cases among women (CDC, 2002). Research has overlooked HIV-positive Latinas in particular, despite the facts that HIV infection is the fourth leading cause of death among Hispanic women (CDC, 2004), that Latino men have HIV case rates that are three times higher than those of Caucasian men, and that Latinos, compared to other ethnicities, have the lowest rate of condom use efficacy (Zambrana, Cornelius, Boykin, & Salas-Lopez, 2004). Socioeconomic and ethnicity-related factors such as lack of insurance and transportation, discomfort with sex-education programs designed for English-speakers, and concerns about confidentiality and social stigma are additional barriers to receiving HIV
screening and prevention services. It is further hypothesized that Latinos’ greater prevalence of HIV may be due to cultural-specific beliefs that sexual knowledge may promote sexual activity and religious beliefs in virginity and abstinence until marriage (Talashek, Peragallo, Norr, & Dancy, 2004). These cultural beliefs about sexuality and condom use put Latinas at even further risk for the development of gynecological problems such as sexually transmitted infections (STIs), cervical dysplasia, and yeast infections. As research demonstrates that Latinas, in comparison with other women of color, tend to put a greater emphasis on the roles of marriage and motherhood (East, 1998) and to detrimentally idealize romantic relationships (O’Sullivan & Meyer-Bahlburg, 2003), looking at how close relationships affect the trajectory of HIV is an important factor in understanding why HIV has increased so dramatically in heterosexual women.

**Depression and Immune Health**

*Women and Relationships*

Studies have shown that among HIV-positive women the prevalence of depression is at least twice as high as among their HIV-positive male counterparts (Evans et al., 2001), ranging from 30 to 60% in community samples (Morrison & Evans, 2002, Ickovics et al., 2001). These findings are not surprising when considering the consistent documentation of gender differences in the prevalence rate of depression generally (e.g. Kessler et al., 1994; Kornstein, 1997), with most of the data suggesting that depression in women is typically 2 to 3 times the rate among men. Thus, as women are at higher risk for depression, HIV infection thus seems to not only increase vulnerability to depressed mood in its own right, but to also secondarily “[expand] the range of chronic burden to which these low-income seropositive women are vulnerable” (Gurung, Taylor, Kemeny, & Myers, 2004).
Women living with HIV experience numerous psychosocial stressors including social stigma, multiple care-taking roles, financial difficulties, difficulties accessing health care, and perhaps most significantly, the changes that the disease may have on their personal, intimate relationships. As social relationships play a crucial role in promoting effective coping and adjustment to serious chronic illness, conflict within these interpersonal relationships can therefore be negatively associated with psychological adjustment. Women, especially women of color, are usually the primary caretakers of their families (Goggin & Rabkin, 1995). Not only are they caring for themselves and others, they may also be caring for their ongoing romantic relationship. One study found that, after HIV infection notification, 27% of women experienced changes in their intimate relationships, and over two-thirds endured severe difficulties in their sexual relationships (Pergami et al., 1993). Although some studies show that the prevalence of partner conflict does not differ between HIV-positive women and HIV-negative women with similar sociodemographic characteristics, the impact of partner conflict on mental health may be greater among infected women. For example, Milan, Ickovics, Vlahov, Boland, Schoenbaum, Schuman & Moore (2005) reported that partner conflict, maternal role difficulty and social isolation contributed to increased baseline depression in HIV-positive women, but that only partner conflict predicted change in depressive symptoms over time.

**CD4 Cell Count and Gynecological Problems**

Depression is not only a disorder of the mind, it is also a disease of the body. Depressive symptoms are associated with decreased CD4+ cell counts (one of the t-cell types most directly affected by HIV), albeit indirectly via the SNS and HPA axis pathways (Ironson, O’Cleirigh, Fletcher, Laurenceau, Balbin, Klimas, Schneiderman, & Solomon, 2005). When an individual experiences chronic stress, the continued over-activation of the HPA weakens the body’s
immune system, thereby altering immune response and furthering HIV progression via the chronic elevation of cortisol, or hypercortisolemia (Lederman, Rodriguez & Sieg, 2004). This chronic elevation can decrease lymphocyte functioning by reducing the numbers of CD4+ cells (Leserman, 2003). Ultimately, these CD4+ reductions increase viral replication and inhibit immune response to other pathogens, and simultaneously increase risk for opportunistic infections. In a landmark, seven-year PNI study of these depression-HIV connections in women (Ickovics et al., 2001), HIV-positive women with chronic depressive symptoms were two times more likely to die compared with those with limited or no depressive symptoms. This effect was due primarily to the evidence of a more rapid decline in CD4+ cell count in these chronically depressed women compared to their non-depressed counterparts. Depression remained significantly associated with mortality even after somatic symptoms of depression were eliminated, suggesting that rather than simply being artifacts of worsening health, depressive symptoms may independently contribute to HIV-related mortality.

Further, CD4 t-cell count is one of the strongest predictors of the development of STIs in HIV-positive women, via the indirect link of continued corticosteroid and catecholamine activation. Many studies have focused on the associations between CD4 cell count and human papillomavirus (HPV), and have consistently demonstrated that the prevalence and persistence of HPV is linked to a decreased CD4 cell count (e.g. Strickler, Burk, Fazzari, Anastos, Minkoff et al., 2005). HPV is one of the STIs most commonly and persistently experienced by HIV-positive women, and is etiologically associated with the development of cervical dysplasia and cervical cancer (Wyatt, Moe, & Guthrie, 1999; Palefsky, Minkoff, Kalish, Levine, Sacks et al., 1999). As HPV is also associated with age and socioeconomic status, research has found that HPV regression in HIV-positive women is least likely in Latinas, in comparison with African-
American and Caucasian women (Massad, Silverberg, Springer, Evans, Passaro et al., 2004). Although the discovery and treatment of STIs can be perceived as stressors, particularly when one is involved in a romantic relationship, there is little data examining the connections between depression and STI prevalence. One study used multilevel modeling to show that higher life stress increased the odds of having an abnormal Papanicolaou (Pap) smear, with developing progressive and persistent cervical lesions, and acquiring HPV in HIV-positive women over time (Pereira, Antoni, Danielson, Simon, Efantis-Potter et al.; 2003). However, this study focused solely on women of African-American and Caribbean-American descent, and to my knowledge these associations have not been examined in Latina women.

**Relationship Functioning and Immune Health**

*Couple Conflict and HIV*

It has been consistently established that couple conflict is related to psychopathology, heightened blood pressure and heart rate, higher reports of bodily pain, poorer outcomes in rheumatoid arthritis and Epstein-Barr virus, and elevated levels of cortisol, epinephrine, and norepinephrine (Robles & Kiecolt-Glaser, 2003). However, there are relatively fewer studies that have investigated the links between relationship conflict and HIV. Currently, as the vast majority of HIV infections in women stem from sexual encounters in intimate relationships, at its most fundamental level HIV is a disease innately intertwined with relationships. The continually changing nature of HIV and its effects on a person’s health status both parallels and perpetuates changes that may occur in an intimate relationship. As HIV infection affects women’s physical, economic, and social needs, partner conflict may have a robust effect on immune health because the disease’s progression may increase their vulnerability within or dependence upon their partner and their relationship.
Couple Conflict, T-Lymphocytes and Gynecological Problems

Several studies have shown that couple conflict can lead to direct changes in levels of t-lymphocytes. For example, Dopp, Miller, Myers & Fahey (2000) found that following a 15 minute conflict task, couples responded with decreases in the percentage of circulating CD4+ T cells and increases in the percentages of cytotoxic NK and CD8+ cells. In a study of newlyweds (Kiecolt-Glaser, Malarkey, Chee, Newton, Cacioppo & Mao, 1993), hostile and negative behavior during conflictual discussions was associated with elevated levels of epinephrine and norepinephrine, declines in natural killer (NK) lysis, and poorer control of a latent herpes virus by the immune system. In the 10-year follow-up, levels of epinephrine and norepinephrine were elevated among divorced couples compared to married couples, with a greater degree of change in women compared to men.

The fact that even brief, one-time conflictual discussions can lead to detrimental immunological changes is telling and highlights the potential enormity of the longitudinal links between chronic relationship conflict and the cumulative effects of physiological responses to stress. Further, as relatively healthy, non-distressed couples are the primary participants in these studies, these results may actually underestimate the consequences of couple conflict on immunological health. Studying dysfunction in women’s romantic relationships will provide further and unique clarification of the specific conditions wherein women may be at an increased risk for both HIV disease progression and depression.

In order to examine these conditions, I propose to use a sample of (N=149) HIV-positive (N=97) and HIV-negative (N=52) Latinas from the University of California-Los Angeles Charles Drew Medical Center Women and Family Project (WFP; Dr. Gail Wyatt PI), a 5-year longitudinal study examining the impact of HIV on women’s lives (see Wyatt & Chin, 1999).
The participants were assessed and surveyed in person at baseline and every six months over the course of two years, and I will thus be using data from these five time points. I aim to a) test if relationship functioning affects CD$ T-cell count and whether this relationship is mediated by depression in HIV-positive Latinas and to b) test if relationship functioning is associated with higher rates of gynecological problems in HIV-positive and HIV-negative Latinas, and whether these relationships will be moderated by HIV-serostatus and mediated by depression.
REFERENCES


