

## Sleep disturbance mediates the association between psychological distress and immune status among HIV-positive men and women on combination antiretroviral therapy

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### Abstract

**Objectives:** This study examined the relationship between psychological distress, subjective sleep disturbance and immune status among HIV-positive men and women. **Methods:** Fifty-seven participants (41 men, 16 women) without AIDS-related illness and currently on combination antiretroviral therapy were recruited through community advertisement and physician referral. Participants completed the Impact of Events Scale (IES) to assess symptoms of psychological distress and the Pittsburgh Sleep Quality Index (PSQI) to assess quality of sleep over the past month. T-lymphocyte subpopulations were also assessed from

early morning blood samples. **Results:** Participants reporting greater psychological distress also reported more pronounced sleep disruption. Higher levels of distress and greater sleep disturbance were also significantly related to lower T-cytotoxic/suppressor (CD3+CD8+) cell counts. Path analysis revealed that the association between distress level and CD3+CD8+ cell counts was mediated by poorer subjective sleep quality. **Conclusions:** These findings suggest that psychological distress may impact upon the immune system through its effects on sleep quality. © 2003 Elsevier Science Inc. All rights reserved.

*Keywords:* Sleep; Distress; HIV; Immune

### Introduction

Human immunodeficiency virus (HIV) infection is often accompanied by a number of physical symptoms, including sleep disruption. A recent study classified 73% of 115 HIV-positive patients as having a sleep disturbance [1], based upon elevated scores on the Pittsburgh Sleep Quality Index (PSQI) [2]. Sleep disturbances seem to develop soon after initial infection and continue across the disease course. In a study of 50 HIV-positive patients, sleep

impairments were observed across all clinical stages, and increased with advancing disease status [3]. Although these studies provide evidence that sleep problems are common among HIV-positive individuals and may worsen over time, less is known about what precipitates these sleep disturbances. One pathway might involve psychological distress.

HIV-positive individuals often contend with a number of psychological stressors and social challenges, such as financial concerns, impaired autonomy, social stigma, multiple bereavements and numerous other psychosocial stressors. Even with the discovery of newer medications, they must cope with the complex psychosocial demands of this chronic illness and its treatment [4]. These types of recurrent stressors may impact upon their sleep as well as their immune status.

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A number of studies have found relationships between greater distress states and poorer immune status among HIV-positive individuals [5–10], although some studies have not [11,12]. It is possible that the association between distress and immune status is due, at least in part, to distress-induced alterations in sleep quality. Alterations in sleep help explain the effects of distress on various immunologic parameters among healthy individuals. A prior study found that greater distress scores were associated with decreases in the natural killer (NK) cell phenotype, CD3 – CD56+ [13]. This stress–immune relationship was mediated by greater sleep disruption among the more stressed individuals. It is plausible that stress-related sleep disruptions may exacerbate extant immune system impairments in HIV-positive persons [14], though surprisingly little work has examined this association.

Even minimal sleep deprivation has profound effects on the immune system of healthy individuals. A study of 23 healthy men found that NK cell activity was significantly reduced after partial sleep deprivation [15]. Studies examining the restorative effects of sleep following deprivation have found that the production of interleukin-2 (IL-2), stimulated by phytohemagglutinin (PHA), was enhanced [16] and circulating immune cells (e.g., monocytes, NK cells) were significantly higher after restorative sleep [17]. Thus, alterations in sleep patterns, either deprivation or restoration, seem to impact upon immune status.

The current study examined distress and subjective sleep quality and their relationship with two key lymphocyte subpopulations, CD3 + CD4+ (helper/inducer) and CD3 + CD8+ (cytotoxic/suppressor) cells, among HIV-positive men and women on an established course of combination antiretroviral therapy (CART). We hypothesized that individuals experiencing greater psychological distress will report more pronounced sleep disturbances. We also predicted that greater distress level and sleep disturbance would be associated with lower CD3 + CD4+ and CD3 + CD8+ cell counts, and that the distress–immune associations would be mediated by poorer sleep quality.

## Method

### *Participants*

HIV-positive men and women were recruited through advertisements and physician referral. In order to study a contemporary and relatively healthy sample, we selected only those individuals currently on an established regimen (for at least one month) of CART and those without AIDS-defining symptoms or CD3 + CD4+ cell counts less than 200 cells/mm<sup>3</sup>. A total of 57 individuals met criteria for the study, and underwent a physical examination, provided a blood sample for lymphocyte phenotyping, and completed relevant questionnaires.

### *Measures*

#### *Sleep quality*

All participants completed the PSQI, a self-report instrument commonly used to assess sleep quality [2]. The PSQI is a 17-item instrument with most questions rated on a four-point Likert scale, and others that directly ask usual bedtime, amount of time to fall asleep, usual wake-up time and average number of hours of sleep per night. The PSQI has well-established reliability and validity.

#### *Psychological distress*

The Impact of Event Scale (IES) [18] was administered to assess psychological distress. The IES is a 15-item instrument rated on a 4-point Likert scale that taps intrusive and avoidant thoughts regarding stressful events. The IES has well-established reliability and validity, and has been used extensively among a number of medical, psychiatric and community populations.

#### *Immune status*

Peripheral blood samples were collected from all participants to determine CD3 + CD4+ and CD3 + CD8+ cell counts. Samples were collected between 9 a.m. and 12 p.m. using sterile evacuated tubes containing sodium heparin (Vacutainer Catalog #6489, Becton-Dickinson, Rutherford, NJ). A single laser flow cytometer (EPICS C, Coulter Instruments Laboratories, Hialeah, FL) was used along with a whole blood, two-color immunofluorescence [19]. The percentage of cells positively stained for CD3 and CD4, as well as CD3 and CD8, monoclonal antibodies were converted to an absolute count by multiplying by the lymphocyte count obtained from a MAXM hematology counter (Coulter Instruments Laboratories, Hialeah, FL).

## Results

### *Participant characteristics*

Participants consisted of 41 men and 16 women, with an average age of 38.79 (S.D. = 8.48) years. The sample was 26% African–American, 37% Caucasian and 33% Hispanic. Modal income was in the range of US\$10,000–30,000 per year. About 53% were asymptomatic and 47% were symptomatic, non-AIDS. All participants were currently prescribed a CART regimen and 67% were prescribed a protease inhibitor. Most of the subjects (90%) reported drinking beverages containing caffeine and 63% reported consuming three or less cups of coffee (or equivalent beverage) per day. About 69% of the participants reported current alcohol use, of whom the majority (71%) reported drinking one to three alcoholic beverages per week. About 54% of the participants reported currently smoke cigarettes, of whom the majority (90%) smoked one pack of cigarettes per day or less.

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