THE RELATIONSHIP BETWEEN SLEEP, AGE AND PSYCHOMOTOR PERFORMANCE IN OLDER ADULTS WITH HIV

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Abstract

Little is known regarding sleep patterns of older adults with HIV. The primary goal of this study was to utilize multiple methods to assess sleep patterns in an older (50+ years) HIV positive group, and compare them to older HIV negative and younger HIV positive control groups. In addition, the study examined the relation between sleep indices and psychomotor function. Study participants were recruited from a longitudinal neurologic study of HIV positive adults. The participants (38 HIV+ older, 31 HIV- older, and 16 HIV+ younger groups) wore a wrist actigraph to monitor sleep, and completed a sleep diary for the 3 consecutive nights before their annual assessments. They also completed the Pittsburgh Sleep Quality Index (PSQI), which reported typical sleep patterns over the previous month. The older HIV positive participants reported higher rates of disturbed sleep compared to the control groups. Seventy-one % of the HIV+ older group, vs. 39 % of the older HIV- group, and 40 % of the younger HIV+ group reported global PSQI scores in the “sleep disturbed” range. When comparing the older HIV positive group to the control groups, the older HIV positive group had significantly poorer sleep quality than the HIV negative group, as reported by PSQI global score (M = 7.6, SD = 3.6 for HIV positive vs. M = 4.4, SD = 2.8 for HIV negative), and sleep diary (M = 2.9, SD = 0.84 for HIV positive vs. M = 3.5, SD = .74 for HIV negative). There was no significant difference between the older HIV+ group and younger HIV+ group for any of the reported sleep variables. There were no significant differences between the older HIV+ group and control groups for total sleep time, sleep onset latency, number of
awakenings, sleep efficiency. In linear regression models, aggregated measures of sleep quality did not account for a significant amount of the variance in an aggregated measure of the psychomotor scores. While there were no differences between the older HIV positive group and the control groups for quantitative sleep measures, the older participant group clearly experienced poorer perceived sleep quality.
Table of Contents

Acknowledgements........................................................................................................ 2
Abstract............................................................................................................................ 3
List of Tables..................................................................................................................... 8

Chapter 1

Introduction....................................................................................................................... 9
  Sleep Disturbances in HIV......................................................................................... 12
  Consequences of Sleep Loss....................................................................................... 15
  Psychomotor changes in HIV..................................................................................... 16
  The Relationship between Aging, Sleep and Psychomotor Changes......................... 20
    Aging and Sleep........................................................................................................ 20
    Cognitive Changes in older adults with and without HIV........................................ 22
    Sleep and Cognition in older adults with and without HIV....................................... 25
  Study Goals............................................................................................................... 27

Chapter 2

Method............................................................................................................................ 27
  Background.................................................................................................................. 27
  Overview of Methods................................................................................................ 28
  Participants.................................................................................................................. 29
    Hawaii Aging with HIV Cohort............................................................................... 29
      Recruitment............................................................................................................ 29
      Demographics....................................................................................................... 29
Study Goal 1: Descriptive Statistics........................................ 49
  Sleep Data............................................................................49
Study Goal 2: Between Group Analyses of Sleep Dimensions......... 52
  Aggregation of Sleep Indices................................................54
Study Goals 3 & 4...................................................................56

Chapter 4
Discussion..............................................................................61
References..............................................................................67
Appendix A: Sleep Diary..........................................................83
Appendix B: Pittsburg Sleep Quality Index (PSQI).............................85
Appendix C: Scoring Instructions for the Pittsburgh Sleep Quality
  Index.....................................................................................87
Appendix D: Neuropsychological Battery for the Aging with HIV
  Study.....................................................................................91
Appendix E: Sleep Study Flyer....................................................92
Appendix F: Letter sent to older HIV Negative Participants..............93
Appendix G: Sleep Study Visit Protocol......................................94
Appendix H: Informed Consent..................................................95
Appendix I: Actiwatch Instructions..........................................99
Appendix J: Sleep Study Pamphlet............................................100
Appendix K: Form Letter to Primary Care Physician.....................102
Appendix L: Glossary of Medical Terms.....................................103
List of Tables

1. Demographic Data, HIV Characteristics, and Neuropsychological Test Scores for Sleep Study Participants…………………………………...34

2. Mean Scores* and Standard Deviation Scores for Sleep Questionnaires…………...50

3. Intercorrelations between Subjective and Objective Sleep Measures…………55

4. Means, Standard Deviations, and Correlations Among Regression Variables…. 58

5. Summary of Regression Analysis (full and restricted models)…………………... 59

A. Summary of Epidemiologic Sleep Studies in HIV Research…………………..105
CHAPTER 1

Introduction

Both disturbed sleep and cognitive impairment are well documented in adults with Human Immunodeficiency Virus (HIV). Compared to adult community samples, higher rates of sleep disturbance are commonly reported in HIV positive adults (e.g., Ford & Kamerow, 1989; Ohayon, 1996; Wheatley & Smith, 1994). For example, one study reported 73% of HIV positive participants (N = 115) were classified as having disturbed sleep during the previous month (Rubinstein & Selwyn, 1998). In comparison, only 34.5% of a sample of 112 community volunteers (participating in a study of circadian cycles) reported similar sleep disturbances¹ (Grandner, Kripke, Yoon, & Youngstedt, 2006). While HIV infection appears to affect a variety of cognitive domains, such as executive skills, information processing speed, language/verbal functioning, immediate and delayed visual memory, visual construction and attention/concentration, studies of adults with HIV have reported psychomotor slowing to be one of the more consistent and early impairments in cognitive function (Goodkin et al., 2001; Reger, Welsh, Razani, Martin, & Boone, 2002). In general, declines in sleep quality and psychomotor slowing are initially minimal or absent immediately post infection, and become more profound as HIV infection progresses and becomes more symptomatic (Goodkin et al., 2001; Reger, Welsh, Razani, Martin, & Boone, 2002; Sciolia, Atkinson, & Grant, 1998).

¹ Sleep disturbances for Rubenstein & Selwyn (1998) and Grandner et al., (2006) were defined as scores of above 5 on the Pittsburgh Sleep Quality Index (Buysee, Reynolds, Monk, Berman, & Kupfer, 1989).
Sleep loss may contribute directly to psychomotor slowing, and may also be associated with a variety of other negative consequences. Sleep restriction/deprivation studies with healthy adults demonstrate that sleep loss can result in deficits in several cognitive domains, such as reaction time, vigilance, concentration, and memory (Dinges et al., 1997; Morin, 1993; Veasey, Rosen, Barzansky, Rosen, & Owens, 2002). In addition, sleep loss can result in mood disturbances (Ford & Kamerow, 1989; Morin, 1993), poorer perceived quality of life (Leger, Guilleminault, Dreyfus, Delahaye, & Paillard, 2000), and poorer health outcomes (Morin, Culbert, & Schwartz, 1994).

Psychomotor slowing is significantly associated with negative outcomes in HIV positive individuals, and may be one of the earliest indicators of overall cognitive decline. Psychomotor slowing has been significantly associated with a later diagnosis of dementia, early mortality (Bouwman et al., 1998; Dunlop et al., 2002; Sacktor et al., 1996; Selnes et al., 1995) and poor medication adherence (Hinkin et al., 2004). In addition, measures of psychomotor slowing may be more sensitive than other neuropsychological measures at detecting early decline in HIV (Llorente et al., 1998), and early detection may help identify individuals amenable to early treatment with anti-retroviral medication (Sacktor et al., 2003).

The Centers for Disease Control (CDC) and Hawaii State Department of Health report a growing proportion of adults over 50 years old, who are living with HIV or AIDS. The CDC reported that the proportion of AIDS cases in the U.S. in individuals 50 or older increased from 10% in 1995 to 16.3% in 2007 (Centers for Disease Control, 1995, 2007). In Hawaii, the yearly incidence is higher than national estimates, with 27% of newly diagnosed AIDS cases 50 or older in 2007 (Hawaii State Department of Health,
In 2008, 22% of new AIDS cases reported in Hawaii were with individuals 50 years or older (Hawaii State Department of Health, 2009).

The relation between sleep, psychomotor slowing and HIV is difficult to estimate, particularly in older adults. In non-clinical community samples, aging is significantly associated with greater rates of subjective sleep disturbances (e.g., Foley et al., 1995), and subjective sleep complaints are also associated with cognitive decline (Hart, Morin, & Best, 1995; Jelicic et al., 2002). Several longitudinal HIV research groups have recently studied the relation between aging and cognitive function, and there is evidence that age is an independent risk factor in the development of HIV-Associated Dementia (Valcour et al., 2004). Several sleep studies have analyzed the effect of age on sleep disturbance in their HIV positive participant groups, and thus far have not found a significant relation (Cohen, Ferrans, Vizgirda, Kunkle, & Cloninger, 1996; Nokes & Kendrew, 2001; Vance & Burrage, 2005; Wheatley & Smith, 1994).

To date, little is known regarding sleep patterns of older adults with HIV, or how they might relate to cognitive impairment in general, and specifically, psychomotor slowing. While sleep research with HIV positive individuals has included some older adults, the mean age for participant groups in most studies is 35-40 years, and often includes few individuals in their 50’s or older (e.g., Cruess et al., 2003; Rubinstein & Selwyn, 1998; Wheatley & Smith, 1994). This study assessed sleep in a sample of older HIV positive adults, utilizing both objective and subjective measures, and compared sleep indices with older HIV negative and younger HIV positive control groups. In addition, the relation between older HIV positive adults sleep and psychomotor slowing was examined.
Disturbed sleep is well documented in HIV positive adults. Table A reports results of sleep studies in HIV positive groups. Several researchers have used the Pittsburg Sleep Quality Index (PSQI)\(^2\), to estimate prevalence of sleep disturbances in HIV. Using a PSQI global score of greater than 5 as a cutoff to categorize poor sleepers, researchers found 61.4% and 73% participants with HIV could be classified as having disturbed or poor sleep (Cruess et al., 2003; Rubinstein & Selwyn, 1998). PSQI mean global scores of 6.72 (SD = 3.82), 9.0 (SD = 4.4) and 10 (SD = 5) have also been reported for HIV positive adults (Cohen et al., 1996; Cruess et al., 2003; Nokes & Kendrew, 2001). The mean scores for the HIV positive groups are considerably higher than those obtained for a group of normal sleepers (2.67 [SD = 1.7]) in a study evaluating the psychometric properties of the PSQI (Buysee et al., 1989), and are closer to mean scores obtained for a group of patients diagnosed with sleep disorders\(^3\) (10.38, SD = 4.57) from the same study.

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\(^2\) The PSQI yields a global score which ranges from 0-21, with higher scores indicating greater sleep disturbances. Developers of the PSQI recommend using a cutoff score of >5 to distinguish between “good” and “poor” sleepers (Buysee, Reynolds, Monk, Berman, & Kupfer, 1989).

\(^3\) Sleep disorder patients were diagnosed with disorders maintaining and/or initiating sleep, according to Association of Sleep Disorders Center (ASDC) criteria (ASDC, 1979; cited in Buysee, et al., 1989).
Several studies have also surveyed specific sleep-related complaints in HIV positive individuals. According to a review of the neuropsychiatric features of HIV, the most commonly reported sleep-related complaints are: difficulty maintaining sleep, not feeling refreshed upon wakening, and the need to take daytime naps (Sciolla, Atkinson, & Grant, 1998). For example, a 2004 study of 125 HIV positive adults (mean age = 40 yrs) found that 33% of participants reported having a disturbed night’s sleep three or more days per week, 29% reported waking too early three or more days per week, and 40% reported poor sleep quality. In addition, this study also reported more than 31% of respondents had difficulty falling asleep three or more nights per week (Hodges & Buboltz, 2004).

One body of research has focused on the relation between sleep disturbances and the progression of illness associated with HIV, with inconsistent results. At least 2 studies reported a significant association between CD4+ counts and sleep indices (Darko, McCutchan, Kripke, Gillin, & Golshan, 1992; White et al., 1995). For example, White and colleagues (1995) found that CD4+ counts of > 400 x 10⁶/l were associated with significantly fewer awakenings in asymptomatic HIV positive men when compared with HIV negative controls (White et al., 1995). Conversely, other studies have reported that CD4+ cell counts were not significantly related to subjective sleep or fatigue measures (Cruess et al., 2003; Lee et al., 2001). When examining CDC disease stage categories in HIV and sleep, at least two studies report significantly higher rates of sleep disturbance in later stages of HIV infection, but not in earlier stages. This increase may

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⁴ CD4: A membrane protein or receptor of T-helper lymphocytes; is the attachment site for HIV (Kalichman, 1998).
be more related to symptoms associated with AIDS-defining illness rather than CDC stages per se (Reid & Dwyer, 2005). For example, Nokes and Kendrew (2001) reported that sleep quality was significantly related to symptom severity ($r = .45$), although no significant relation was seen between sleep quality and AIDS diagnosis or CD4+ count. Several studies have also examined CDC stages or AIDS diagnosis and have found no relation to reported sleep patterns (e.g., Brown, Mittler, & Atkinson, 1991; Cohen et al., 1996; Lee et al., 2001; Nokes & Kendrew, 2001; Rubinstein & Selwyn, 1998; Wheatley & Smith, 1994).

There are several possible explanations for increased sleep complaints in HIV positive individuals. Community studies consistently report higher rates of sleep disturbances in individuals with depressive or anxiety symptoms, or self-reported body pain (e.g., Oyayon, 2009; Stepanowski & Ancoli-Israel, 2008). For example, in a prospective study of 464 self reported good sleepers (upon entry to the study), authors reported that a previous episode of insomnia, a family history of insomnia, higher depressive and anxiety symptoms, higher self-reported bodily pain, and poorer self-reported health were significantly related to new incidence of insomnia during the course of the study (LeBlanc et al, 2009). A higher incidence of pain and depression (compared to community samples) are well documented in the HIV positive population (e.g., Tsao & Soto, 2009; Komiti et al., 2003). In a review of sleep studies in HIV infection, Reid & Dwyer (2005) reported that cognitive impairment, AIDS-defining illness, Efavirenz, and depression or anxiety appeared to be risk factors for insomnia in HIV. According to Reid & Dwyer (2005), the most robust relationship for risk of sleep complaints was with depression or anxiety (Reid & Dwyer, 2005).
In summary, HIV positive individuals often experience significantly higher rates of sleep disturbances than reported in the general population. The most commonly reported sleep disturbances include difficulty falling and/or maintaining sleep, subjectively poor sleep quality, and frequent daytime naps. Several studies have demonstrated an increase in sleep-related difficulties as HIV progresses.

Consequences of Sleep Loss

Sleep disturbances can affect daily and long term functioning in a number of ways. Studies of partial and total sleep deprivation have demonstrated that loss of sleep increases daytime sleepiness (Carskason & Dement, 1979; Roth, Roehrs, Carskadon, & Dement, 1994), and can result in the emergence of microsleeps (periods of a few seconds of sleep) during the day (Hauri, 1982). For example, Carskadon & Dement (1981) found that Multiple Sleep Latency Scores5 changed from an average of 17 minutes (SD = 3) during baseline measurement to 7 minutes (SD = 4) after 7 nights of sleep restriction. Sleep loss can also impair performance on highly creative or monotonous tasks (Balkin & Badia, 1988; Gillberg, Kecklund, & Torbjorn, 1994; Hauri, 1982), negatively impact other cognitive functions (e.g., concentration, memory, creativity, perception, judgment, reaction times), impair decision making (Morin, 1993), decrease motivation (Horne, 1988), and depress mood (e.g. irritability) (Morin, 1993; Totterdell, Reynolds, Parkinson, & Briner, 1994). Sleep loss can also result in more somatic complaints, days of sick leave, greater utilization of health care resources (Morin et al., 1994), and increased risk of mortality (Gallicchio & Kalesan, 2009). In HIV, sleep disturbance may also have a

5 Individuals are offered several naps at 2 hour intervals during the day, and the speed at which they fall asleep is measured (Morin, 1993).
Sleep and psychomotor slowing in older HIV

negative impact on medication adherence (Phillips et al., 2005). Finally, a large community study (N = 1053) reported that participants who met criteria for insomnia (as defined by the DSM IV) had significantly worse scores on a measure of quality of life (for subscales physical functioning, bodily pain, perceived general health, vitality, social functioning, emotional well-being and mental health) when compared to good sleepers (Katz & McHorney, 1998; Leger, Scheuermaier, Philip, Paillard, & Guilleminault, 2001).

In summary, studies of healthy adults have demonstrated that loss of sleep can significantly impair daily functioning, including cognitive functions such as memory, concentration, reaction times and judgment. In addition, these studies have demonstrated that sleep loss can result in greater health concerns and poorer overall quality of life.

Psychomotor changes in HIV

Research on HIV positive adults has demonstrated that cognitive changes are often minimal in asymptomatic HIV positive individuals, with decrements becoming more pronounced as HIV progresses and becomes more symptomatic (e.g., Goodkin et al., 2001; Hardy & Hinkin, 2002; Reger et al., 2002). Reger and colleagues (2002) reviewed 41 studies (N = 8616) comparing neuropsychological measures between HIV negative and HIV positive groups6. Using Cohen’s $d$ to calculate the magnitude of

6 The HIV positive groups were defined as follows: (1) Asymptomatic HIV positive, (2) Symptomatic HIV positive, including patients that displayed symptoms indicative of HIV infection such as chronic low grade fever, persistent fatigue, diarrhea, rashes, unintentional weight loss, and do not meet criteria for a diagnosis of AIDS, and (3) HIV positive patients with an AIDS diagnosis defined by a CD4 count of less than 200
between-group comparisons, they found that effect sizes increased as a function of
disease severity, and all three groups (asymptomatic, symptomatic, and AIDS groups of
HIV positive participants) differed significantly from HIV negative controls. The effect
sizes were small when comparing asymptomatic HIV positive individuals to HIV
negative controls, with 0.07 for motor function tests (including Grooved Pegboard), and
0.14 for information processing tests (including the Digit Symbol and Trail Making
tests). Effect sizes were larger when comparing asymptomatic HIV positive participants
to HIV positive participants with more advanced disease symptoms (i.e., symptomatic),
with symptomatic HIV positive participants earning significantly poorer scores on tests
of psychomotor functioning (.58), executive skills (.34), information processing speed
(.33), language/verbal functioning (.27), delayed visual memory (.22), and immediate
verbal memory (.16) than asymptomatic HIV positive participants.

While patterns of neuropsychological performance can be variable (Dawes et al.,
2008), psychomotor slowing is often detectable early in HIV infection, and may be a
more sensitive indicator of cognitive decline than other neuropsychological measures. In
the Multi-Center AIDS Cohort Study (MACS), symptomatic HIV positive participants
demonstrated significantly greater slowing in tests of motor speed and manual dexterity\(^7\)
\((F = 46.6 \text{ to } 107.1, \ p = <0.001)\), simple and complex psychomotor functioning \((F = 25.1
\text{ to } 34.4, \ p = <0.001)\), and simple and complex cognitive processing \((F = 8.5 \text{ to } 66.7, \ p = <0.01)\), when compared to HIV negative controls. In the asymptomatic HIV positive
cells/mm\(^3\), or the presence of an AIDS defining condition, such as Kaposi’s Sarcoma,
Cytomegalovirus, Burkett’s or Immunoblastic Lymphoma, etc (Kalichman, 1998).

\(^7\) Authors report F statistics only, not effect sizes.
patients, no significant differences were found between the positive and negative groups with the exception of a single psychomotor test, the Grooved Pegboard ($F = 4.91$ for dominant and 5.74 for non-dominant, $p < 0.05$) (Llorente et al., 1998). In another study, Parsons and colleagues (2007) reported that a short psychomotor battery was able to distinguish between HIV positive adults with and without cognitive impairment\(^8\) with a sensitivity of 0.79 and specificity of 0.76 (rates equivalent to their significantly longer comprehensive battery). The psychomotor battery, including timed gait, Grooved Pegboard, Fingertapping, Digit Symbol and Trailmaking tests accounted for 73% of the variance in a comprehensive battery that contained psychomotor, attention/concentration, visuospatial, memory, executive function and language-related tests (Parsons et al., 2007).

Another factor that may impact the measurement of cognitive symptoms/impairment is the presence of depressive symptoms. Several studies have demonstrated high correlations between depressive symptoms and neuropsychological testing, although literature is inconsistent, and some studies have found no significant association (McClintock, Hasain, & Greer, 2010). In older adults, the Maastricht Aging Study (MAAS; $N = 598$) examined the relationship between depression scores and neuropsychological test scores, and reported that participants who were persistently highly depressed over time showed significant declines in memory ($P < .001$), processing

\(^8\) Ratings of cognitive impairment were based on the Memorial Sloan Kettering (MSK) dementia scale. The scale utilizes data from neurological, neuropsychological, and quality of life (ability to engage in activities of daily living) measures (Parsons, Rogers, Hall, & Robertson, 2007).
speed ($P = .002$), and global cognition ($P = .01$) compared to participants who were absent of depression (Kohler et al., 2010). In HIV research, a recent study examined the relationship between HIV status, depression and a cognitive score$^9$. Authors reported that that participants with moderate to severe depression had significantly lower cognitive scores than those who were not depressed ($F = 6.3, P < 0.003$), regardless of HIV status (Waldrop-Valverde, Ownby, & Kumar, 2005).

Early signs of psychomotor slowing may predict the development of HIV dementia and HIV encephalitis, or poor prognosis in general (Bouwman et al., 1998; Dunlop et al., 2002; N. C. Sacktor et al., 1996; Selnes et al., 1995). In a longitudinal cohort of 291 men, participants with sustained psychomotor slowing were at increased risk of developing dementia (Risk Ratio [RR] = 5.0, $p = 0.008$), AIDS (RR = 2.4, $p = 0.02$), and death (RR = 2.0, $p = 0.04$)(Sacktor et al., 1996). Sustained psychomotor slowing was defined as a 2.0 standard deviation decline on either the Trailmaking test or Symbol Digit Modalities test on two consecutive assessments (Sacktor et al., 1996). Dunlop and colleagues also found that slowed reaction time 1-2 years prior to death, or at the time of a diagnosis of AIDS, were significantly associated with the development of HIV dementia and HIV encephalitis in 100 AIDS patients (Dunlop et al., 2002).

In summary, cognitive decline tends to be minimal in early or asymptomatic HIV infection, with more profound impairments reported as HIV infection progresses and becomes more symptomatic. Psychomotor slowing may be detected earlier in HIV

$^9$ The cognitive score was based on an aggregate of the following test scores: RCF delayed recall, RAVLT delayed recall, Digit Symbol, Color Trails test 2, Verbal fluency, and Grooved Pegboard, dominant hand (Waldrop-Valverde, Ownby, & Kumar, 2005).
infection than other cognitive domains and may be sensitive to detecting overall cognitive decline. Depressive symptoms may be associated with poorer scores on neuropsychological tests. Finally, the detection of psychomotor slowing may be predictive of the development of dementia, and poor prognosis.

The Relationship between Aging, Sleep and Psychomotor changes

Aging and Sleep

While little is known about sleep changes specific to older adults with HIV, sleep in older community-dwelling adults has been examined in several large scale surveys. Aging is associated with changes in sleep physiology, resulting in gradual reductions in slow wave sleep, REM sleep and sleep efficiency after the age of 40, and increases in Primary Sleep Disorders (Vaz Fragoso & Gill, 2007). In addition, greater rates of self-reported sleep disturbances are reported in older adults. For example, a three community study (N = 9282) of sleep in people aged 65 or older found that 19% reported difficulty initiating sleep, 29% reported difficulty maintaining sleep, 18% reported early morning awakenings “most of the time” (Foley et al., 1995). Using the Pittsburg Sleep Quality Index, a group of healthy older adults (N = 110) reported a mean PSQI global score of 4.3, with 16% of men and 33% of women endorsing PSQI global scores of above 5 (Vitiello, Larsen & Moe, 2004). In comparison, 10.2 % of the National Institute of Mental Health Epidemiologic Catchment Area Study participants (N = 7954, 52% of the
respondents were under 44 years of age) reported having a problem falling or staying asleep for at least 2 weeks during the past 6 months\textsuperscript{10} (Ford & Kamerow, 1989).

Vance & Burrage, 2005, collected data on sleep for an older group of 50 HIV positive adults (ages 31-56, mean age 44.5) and examined the relation between sleep and age. They asked participants to report their usual amount of sleep per night, in addition to the following questions related to sleep: (1) Do you use sleep medications, (2) Do you sleep continuously through the night, (3) Do you have insomnia, (4) Do you wake up feeling rested or fatigued? The authors found no significant differences in reported sleep data between the HIV positive group and an age matched HIV negative comparison group. However, this study is limited in several ways. The age range and mean age of the group was younger than the commonly accepted age of 50 + in HIV research to designate “older” adults. In addition, the sleep questions were retrospective and global, and may have missed information related to specific aspects of sleep. For example, a study of sleep in older women found no significant association between total hours of sleep and cognitive function, but did find significant associations between several other sleep variables (e.g., sleep onset latency, number of naps) and cognitive function (Blackwell et al., 2006).

In summary, sleep reports of older, community-dwelling adults have suggested that subjective difficulties with initiating and maintaining sleep can increase with age, leading to decreased sleep efficiency. To date, sleep research in older adults with HIV

\textsuperscript{10} Sleep disturbances were not a result of physical illness, medication, or drug or alcohol use, and the respondent stated that it interfered with his/her life, took medication for it, and told a professional about it (Ford & Kamerow, 1989).
Sleep and psychomotor slowing in older HIV

has not examined more specific sleep indices. A study of adults 50 years or older using objective sleep measures and a prospective design may yield more precise information regarding sleep in older adults with HIV, and the relationship between sleep, age, and HIV.

Cognitive changes in older adults with and without HIV

In older adults without HIV, psychomotor changes can be sensitive indicators for early stages of cognitive decline, and less sensitive (than other cognitive domains) to the confounding effects of education (Kluger, Gianutsos, Golomb, Ferris, & Reisberg, 1997). Kluger et al., (1997) found that composite scores of fine motor tests (Purdue and Grooved Pegboard tests) and more complex tests of psychomotor function (including WAIS-R Digit Symbol) were able to distinguish cognitively normal adults from mildly cognitively impaired adults (65% and 79% of the time, respectively). They were also able to distinguish cognitively normal adults from adults with mild Alzheimers Disease 74% and 92% of the time, respectively. A composite score of memory and language tests had discriminative power similar to complex motor scores (i.e., 80% and 93% respectively). However, education was more highly associated with the memory and language tests (r = .35 to .54, respectively), compared to no significant association with any of the psychomotor tests (r = -.17 to .27) (Kluger et al., 1997).

In non-clinical community samples, several studies have reported a significant association between subjective sleep complaints and cognitive impairment in older adults (Cricco, Simonsick, & Foley, 2001; Hart et al., 1995; Nebes, Buysse, Halligan, Houck, & Monk, 2009). In a community based study, subjective sleep complaints in older adults (>50 years) were significantly correlated with cognitive decline, as measured by the Mini
Sleep and psychomotor slowing in older HIV

Mental Status Exam (Jelicic et al., 2002). In another study, Hart and colleagues (1995) reported that subjective sleep disturbance was related to poorer performance on tests of vigilance ($R^2 = .15, p = .01$), psychomotor speed ($R^2 = .5, p = .05$), recall memory ($R^2 = .06, p = .05$), and executive function ($R^2 = .13, p = .01$) in an elderly group of patients with insomnia. The Hawaii Healthy Heart study, a prospective study of aging in Japanese-American men, reported that participants (age 71 to 93) were twice as likely to be diagnosed with dementia at a 3 year assessment if they reported daytime sleepiness at the baseline assessment (Foley et al., 2001). Finally, a community study of elderly women (mean age 84 ± 4 yrs) reported significant correlations between several actigraph measures of disturbed sleep (lower sleep efficiency, longer sleep onset latency and longer periods awake during the night) and poorer scores on the Mini Mental State Exam or the Trails B test.\footnote{Adjusted for age, race, depression, education, BMI, history of stroke or hypertension, functional status, alcohol/nicotine/antidepressant use, and physical activity (Blackwell et al., 2006).} (Blackwell et al., 2006). For example, individuals with sleep efficiency of less than 70% had a significantly higher risk of having a Trails B score 1.5 SD or more above the mean (Multivariate Odds Ratio = 9.15; 2.41, 28.73). There was no significant correlation between total sleep time and cognitive measures.

Age may independently increase the risk for cognitive impairment in HIV. Comparing a group of older (50+ years, N = 106) HIV positive individuals with a group of younger (20-39 years, N = 96) HIV positive individuals, Valcour et al., (2004) reported a two-fold increase in risk of HIV-Associated Dementia (Odds Ratio = 2.13, 95% CI = 1.02 to 4.44). Another study followed 290 HIV positive and 124 HIV negative
individuals and found significant differences in the prevalence, but not the one-year incidence of cognitive status related to age. The authors found that mild cognitive impairment was more prevalent in the group under 50 (22% vs. 14% for the older group), and dementia was more common in the group 50 or older (23% vs. 9% for the younger group). In addition, the authors found that the risk of being diagnosed with dementia increased significantly with a history of alcohol abuse/dependence (relative risk [RR] 5.81, 95% CI 1.13-27.1), decreased significantly with higher education (RR 0.26, 95% CI 0.12-0.57), and the viral load was higher at study entry among individuals subsequently diagnosed with impairment ($t_{[110]} = 1.80, P = 0.03$, one-tailed; Becker, Lopez, Dew, & Aizenstein, 2004). Some studies have found no significant interaction effects between HIV and age (Becker, Lopez, Dew, & Aizenstein, 2004; Kissel, Pukay-Martin, & Bornstein, 2005; Vance, Woodley, & Burrage, 2007).

Both age and psychomotor slowing have been found to be significantly associated with poor medication adherence (Barclay et al., 2007; Hinkin et al., 2004; Waldrop-Valverde et al., 2006). A study of 148 HIV positive adults (age range = 25-69) reported that older adults (50+ years) had significantly better medication adherence than younger adults with (87.5% versus 78.3%, respectively)$^{12}$ (Hinkin et al., 2004). Of the older group, adherence was significantly related to scores on the neuropsychological battery, particularly in the area of executive function, memory, and psychomotor speed (e.g., 78%)

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$^{12}$ Participants were considered to be medication adherent if they adhered to the medication regimen 95% of the time (Hinkin et al, 2004)
of individuals with poor adherence were impaired in psychomotor speed\textsuperscript{13}). Another study of 185 HIV positive adults found that younger adults demonstrated poor adherence twice as much as older adults (68\% and 33\% respectively)(Barclay et al., 2007). Among older adults (age 50\+), neurocognitive function predicted poor adherence while low self-efficacy and lack of perceived treatment utility predicted poor adherence in the younger group (Barclay et al., 2007).

In summary, age appears to increase risk of cognitive impairments in both HIV positive and HIV negative adults. Psychomotor changes may be early sensitive indicators of overall cognitive decline in older adults regardless of HIV status. In addition, psychomotor slowing is also a symptom associated with poorer medication adherence in older HIV positive patients, but not younger HIV positive patients.

\textit{Sleep and Cognition in older adults with and without HIV}

While there is little information available regarding the relationship between sleep and cognitive functioning in older adults with HIV, one study found significant correlations between sleep disturbances and some measures of cognitive and psychomotor impairment (Vance & Burrage, 2005). Vance & Burrage (2005) found that

\textsuperscript{13} Impairment was defined as follows: Test scores were converted to demographically corrected T scores with a mean of 50 and a standard deviation of 10, using published normative data. Deficit scores were then calculated using T scores as follows: T \leq 39/4 0; 39 > T > 35 1/4 1; 34 > T > 30 1/4 2; 29 > T > 25 1/4 3; 24 > T > 20 1/4 4; T \leq 20 1/4 5. Participants were classified as ‘impaired’ if the average deficit score for the neuropsychological tests comprising that domain was greater than or equal to 0.5 (Hinkin et al, 2004)
participants who self-reported insomnia vs. those who reported no insomnia had significantly poorer scores on a visuo-spatial task (Rey-Ossterieth Complex Figure copy; \( r = .31, p < .05 \)). In addition, participants that reported use of sleep medications vs. those who reported no use of sleep medications, had better scores on a measure of psychomotor functioning (Trail Making, Part A; \( r = -.35, p < .05 \)), and those reporting fewer hours of sleep per night had higher Rey-Ossterieth Complex Figure copy scores \( (r = .37, p < .01) \).

It is difficult to draw conclusions based on these retrospective data, and a study including more specific and contemporaneous sleep measures, with a more representative older group of HIV positive patients, would facilitate a deeper understanding of this relationship.

Finally, a sleep manipulation study suggested a relationship among age, sleep and psychomotor functioning. Blatter et al. (2006) tested gender and age differences in a psychomotor vigilance task under controlled conditions of sleep deprivation and sleep satiation. They found significantly longer reaction times for women than men, regardless of the age or sleep condition (median reaction time : \( F_{1,10} = 2.3, P < 0.03 \)). Age effects varied, depending on the time of day and amount of sleep deprivation. In general, the older group showed significantly slower reaction times during the day, but not at night, and under conditions of less than 16 hours sleep deprivation, but not over 16 hours sleep deprivation (Blatter et al., 2006).
Study Goals

The specific goals of this study were to: (1) describe the frequency and types of sleep disturbances in older adults with HIV, (2) compare sleep dimensions\textsuperscript{14} and demographic variables of older HIV positive adults to those of younger HIV positive adults and older HIV negative adults, (3) examine the relations between age, sleep and psychomotor functioning in this population (i.e., to examine the degree to which age and sleep account for variance in psychomotor functioning), and (4) examine the degree to which age and sleep account for variance in psychomotor functioning over and above variables likely to moderate this relationship, such as length of infection, CD4, education level, gender and depression.

CHAPTER 2
Method
Background

This dissertation research was nested within an existing longitudinal study: The Hawaii Aging with HIV Cohort (PI: V. Valcour, MD). The Hawaii Aging with HIV Cohort (called the “Memory Study”) was supported by NINDS grant 1U54NS43049, directed by Dr. Cecilia Shikuma. Dr. Valcour was a junior investigator in the program grant and the Principal Investigator for the Memory study. This study was established in 2001 in collaboration with Johns Hopkins University, to evaluate the epidemiology of neurological complications (predominantly cognitive complications such as dementia) among aging HIV individuals. The study received approval from the Human Studies

\textsuperscript{14} Dimension refers to an quantifiable aspect of a variable. Definitions of terms are drawn from http://www2.hawaii.edu/~sneil/ba/.
Committee at the University of Hawaii at Manoa and the Institutional Review Board of the Queen’s Medical Center.

My involvement in the study began in June 2002, and included neuropsychological testing, gathering medical/demographic information of study participants, and managing data entry for the study. In January 2005, a grant proposal was submitted to the Hawaii Community Foundation, with Dr. Valcour as PI and Kathrine Fast as co-PI. This proposal was conceived to be the basis of this dissertation proposal, with the majority of the design/writing completed by the co-PI. The grant was awarded and funded by the HCF (grant 20050407; Sleep Disturbance in aging HIV-1 Seropositive Individuals). Funding was available to conduct the study until October 2006. The study was approved by the Human Studies Committee (CHS # 13827), effective July 19, 2005 (extension granted until July, 2007). The co-PI had primary responsibility for the overall organization/management of the study, collection of data, supervision of data entry, Human Studies Committee approval, and follow-up with the granting agency. Data collection was completed August 31, 2006. In Sept, 2006, approval was granted by the Clinical faculty of the Clinical Studies Program to utilize the data collected for this dissertation project.

**Overview of Methods**

Sleep study participants were recruited from the longitudinal cohort during the time of their annual evaluations. Individuals who were eligible and willing to participate met with the Co-PI, PI or Memory Study Coordinator 3 to 7 days before their annual evaluation to be fitted with a wrist actigraph. The wrist actigraphs were worn for 3 consecutive nights immediately preceding their annual appointment. Participants were
also instructed to complete a sleep diary for the duration of the actigraphy phase of the study. During their annual exam, which included a neuropsychological test battery, participants completed an additional survey, the Pittsburgh Sleep Quality Index, and additional assessments apart from the dissertation research.

Several participants (N=6) indicated they were willing to complete the sleep questionnaires, but declined to wear the actigraph. These participants were asked to complete the Pittsburg Sleep Quality Index and a sleep diary for the previous night during their annual visit, after informed consent had been obtained.

Participants

Hawaii Aging with HIV Cohort

Recruitment. Participants were recruited from the existing Hawaii Aging with HIV cohort. Individuals were recruited for the Hawaii Aging with HIV study via newspaper ads, through HIV advocate agencies (e.g., Life Foundation, Food Basket) and through word of mouth. Individuals belonging to one of two age groups (between 20 to 40 years for the younger group and 50+ years for the older group) were recruited. HIV negative controls were enrolled as they matched the HIV positive groups for age, education, sex and ethnicity. All eligible participants identified English as their primary language. This cohort includes individuals living with HIV on islands of Oahu, Kauai, Maui, Molokai, and Hawaii. Recruitment of new individuals into the study was discontinued in June 2004 for HIV negative participants and continued until June 2005 for HIV positive participants.

Demographics. The Hawaii Aging with HIV cohort followed 137 older HIV positive, 122 older HIV negative, and 124 younger HIV positive participants annually.
The older HIV positive group was 93% male, with a mean age of 54.4 +/- 4.9 years, and mean education of 15.2 +/- 2.5 years. The younger HIV positive group was 76% male, with a mean age of 34.8 +/- 4.7 years and mean education of 13.5 +/- 2.1 years. The HIV negative control group matched the HIV positive group on age, education, and gender.

Sleep Study participants

Recruitment. Willing participants from the Memory Study were enrolled as they came in for annual assessments. One participant was enrolled in September, 2005, to demonstrate the protocol to research assistants. The remainder of the participants were enrolled between the dates of October 5, 2005 and July 7, 2006. In total, wrist actigraph data was collected for 97 participants (42 older HIV positive, 22 younger HIV positive, and 33 older HIV negative individuals). Recruitment occurred in three phases: (1) From September 2005 through November 2005, recruitment was passive. Flyers were sent with annual visit reminders (total = 69). As participants called to make appointments for their annual visits, research assistants were instructed to ask if they would like to participate in the sleep study. This was not being done uniformly by all research assistants. (2) From Nov 28, 2007, through July 7, 2007, a log was created to track and ensure all eligible participants were asked if they would like to participate in the study. During this time, 134 flyers were sent to participants with letters reminding them of their annual visit. Twenty-three participants were not included because of time constraints (e.g. participant preferred to schedule appointment within 2 to 3 days), or lack of availability of wrist actigraph watches. Twelve participants declined to participate, or agreed to participate, but did not come to scheduled appointments. (3) An additional recruitment step was needed for HIV negative older individuals, since the majority of this
group had terminated official participation in the memory study. Eighty-eight older HIV negative participants who met criteria for the sleep study (and lived on Oahu) were sent a letter (see Appendix F) indicating they were eligible to come for an additional visit. Past participants that contacted us, and were willing to complete sleep data were enrolled. In addition to inclusion/exclusion criteria for the Aging with HIV study, participants who met criteria for current drug dependence (approximately 6% of the cohort) in their initial evaluation, or who had a positive urine drug screen for either methamphetamine/amphetamine or cocaine (< 5% of the cohort), or Beck Depression Inventory score greater than 22 (approximately 4% of the cohort) at the time of annual evaluation were excluded. Participants were enrolled regardless of antiretroviral status.

Demographics. Participants included in the analyses were 85 adults recruited from the Hawaii Aging with HIV Study (38 HIV positive older, 31 HIV negative older, and 16 HIV positive younger individuals). Demographic, HIV characteristics, and neuropsychological test score data were available through the Memory Study. Participants’ ages ranged from 29 to 79 years. Table 1 includes mean and standard deviation values of demographic variables, and data provided by the Hawaii Aging with HIV study (neuropsychological scores, HIV related variables). The older HIV positive group was 90 % male, with 71% reporting completion of post high school education (Associates Degree, Technical Degree or above). The older HIV positive group included 76 % Caucasian, 13 % Hawaiian/Part Hawaiian, 9% Asian or Pacific Islander, and 3 % African American participants. Mean years since participants were confirmed HIV positive was 14.6 +/- 6.5, and 86% had a non-detectable Viral Load at the time of their entrance visit into the memory study. Compared to the older HIV positive group, the
HIV negative control group was 97% male, with 75% reporting completion of post high school education. The older HIV negative group included 55% Caucasian, 28% Asian or Pacific Islander, 10% Hawaiian/Part Hawaiian, and 6% African American participants. There were no statistically significant differences in age or level of education.

The younger HIV positive group was 75% male, with 50% reporting education beyond high school (Associates Degree or above, or Technical Degree). The younger HIV positive group included 44% Caucasian, 19% Hispanic, 25% Asian or Pacific Islander, 6% American Indian/Alaskan, and 6% African American participants. Mean years since participants were confirmed HIV positive was 8.1 +/- 4.8, and 69% had a non-detectable viral load. There were no statistically significant differences in education, CD4 count and viral load between the younger and older HIV positive groups, although the length of time since testing positive for HIV was significantly longer ($R^2 = .188$, $p > .001$) in the older HIV positive group.

When comparing data collected upon entry into the Memory Study, the participants who subsequently enrolled in the sleep study did not differ significantly in gender, age, education, viral load or CD4+ counts from their original “Memory Study” groups. While there were no differences in measurable viral load counts, the younger HIV positive group that enrolled in the sleep study had a significantly lower proportion of
Sleep and psychomotor slowing in older HIV

participants whose viral counts were “undetectable”\textsuperscript{15} compared to the original memory study group (25\% vs. 58\%; $R^2 = .043, p > .01$).

\textsuperscript{15} Viral load is designated as “undetectable” when fewer than 50 copies/ml of HIV RNA are present in the blood sample, an amount not detectable by tests used to measure the virus.
Table 1: Demographic Data, HIV Characteristics, and Neuropsychological Test Scores for Sleep Study Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Older HIV + (N = 38)</th>
<th>Older HIV - (N = 31)</th>
<th>Younger HIV + (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.0</td>
<td>5.9</td>
<td>60.4</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.2</td>
<td>2.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Beck Depression Inventory (range 0-63)</td>
<td>6.86</td>
<td>5.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Years since HIV Positive</td>
<td>14.6</td>
<td>6.5</td>
<td>n/a</td>
</tr>
<tr>
<td>Viral Load (copies/ml)</td>
<td>1785</td>
<td>6880</td>
<td>n/a</td>
</tr>
<tr>
<td>WAIS-R Digit Symbol (Raw Score; range 0-93)</td>
<td>54.0</td>
<td>11.8</td>
<td>53.2</td>
</tr>
<tr>
<td>Grooved Pegboard; Non-dominant (Raw Score in seconds)</td>
<td>76.3</td>
<td>14.3</td>
<td>81.1</td>
</tr>
<tr>
<td>Trail Making Test; Part B (Raw Score in seconds)</td>
<td>68.0</td>
<td>28.6</td>
<td>64.6</td>
</tr>
<tr>
<td>NPZ3ᵃ</td>
<td>.32</td>
<td>.86</td>
<td>.38</td>
</tr>
</tbody>
</table>

(a) averaged z-score of WAIS-R Digit Symbol, Grooved Pegboard, Non-dominant, and Trail Making Test; Part B
Sleep and psychomotor slowing in older HIV

Procedures

Hawaii Aging with HIV Cohort

Potential participants were screened in an initial phone call. Major exclusion criteria for the cohort included: 1) diagnosis of a major psychiatric disorder [e.g., bipolar disorder, schizophrenia, active major depression], 2) head injury with loss of consciousness greater than one hour, 3) opportunistic brain infection, 4) learning disability, and 5) major neurologic disease such as stroke, multiple sclerosis, or current delirium (Valcour et al., 2004).

Eligible participants underwent annual evaluations that included a neuropsychological testing battery, a neurologic exam, blood tests, and self-report data including demographic information, medical history, substance use history, medication history, and current depressive symptomatology (as measured by the Beck Depression Inventory). HIV negative participants completed a total of 3 evaluations before termination from the study (baseline, year 1 annual visit, year 2 annual visit), and HIV positive patients continued annual evaluations for 5 years.

Sleep Study

Between August, 2005 and July, 2006, currently active participants of the Memory Study were notified about the sleep study via flyer (See Appendix E), included with their annual appointment reminder letter sent approximately one month prior to their annual visit. The sleep study flyer gives participants basic information about the sleep study. As participants called for their annual appointments, they were asked if they were willing to participate in the sleep study. The names of volunteers were forwarded to the
PI (KF) and arrangements were made to meet the participant at least 3 days prior to the annual appointment.

Volunteers were scheduled for 2 appointments 3 to 5 days apart (See Sleep Study Visit Protocol: Appendix G). During the first 15 minute appointment, participants were given informed consent (See Appendix H), then instructed on the use of the Actiwatch (See Appendix I) and sleep diary. The second appointment was scheduled for 3 to 5 days after the first appointment, and coincided with the annual memory study visit for the participant. A reminder call was arranged for the day the participant would start wearing the actiwatch 3 days before their appointment.

As part of the annual visit, a neurological and 80-minute neuropsychological evaluation was completed, consisting of 16 tests applicable to the evaluation of HIV-related cognitive abilities and deficits (See Appendix D for a list of measures performed in the battery). The NP battery, in conjunction with the neurological examination, allowed for the determination of cognitive endpoints using American Academy of Neurology criteria. Composite neuropsychological scores were used for cognitive outcome measures.

During the second appointment, participants returned the actiwatch and completed sleep diary. In addition, participants were asked to complete the Pittsburgh Sleep Quality Index. After the questionnaires were completed, participant’s received an informational pamphlet about sleep and ways to cope with sleep disturbances (See Appendix J). An informational letter about the results of the sleep study was also sent to the participant’s primary care physician if requested by the participant (See Appendix K). Finally, the
participant was given a monetary compensation of 10.00 for their part in the sleep study. The sleep study portion of the second visit took approximately 15 minutes to complete.

Measures

A Multimethod Approach to Measurement

Sleep Quality and psychomotor performance were each measured by aggregating scores from multiple, methodologically different, assessment instruments to form a composite measure.

Sleep Quality

Aggregate Measure of Sleep Quality. Correlations between multiple measures of sleep quality were examined to ascertain whether they share sufficient variance to justify their aggregation. The following five sleep scores were compared: 1) the average of the second and third nights of wrist actigraph readings for sleep-onset latency and sleep efficiency, 2) the average of the second and third nights of sleep diary recordings of sleep-onset latency and sleep efficiency, and 3) the global sleep quality score from the Pittsburg Sleep Quality Index. Although there is no established criterion for determining the suitability of aggregating two correlated measures, a correlation of 0.5 was used as the criterion for aggregation, indicating that the components have 25% of their variance in common (Peralta, 1999).

After determining scores suitable to combine, z-transformed raw scores were used to construct aggregate measure of sleep quality.

Wrist actigraph. Estimates of sleep and wake states were derived through continuous monitoring of physical activity with a wrist motion sensor (Actiwatch®-64 Activity Monitor, Mini Mitter, Bend, OR).
Participants wore the wrist actigraph on their non-dominant wrist for 3 consecutive nights (Berger, et al., 2008; Sadeh, Hauri, Kripke, & Lavie, 1995). Monitoring was continuous (24 hours/day), and mean scores for the 2nd and 3rd night were reported and used for data analysis (Tyron, 2004). In addition, participants were asked to press an “event marker” twice each day on the actigraph that indicated: (1) bedtime - when the participant first turned out the lights with the intent to fall asleep, and (2) sleep end - when the participant finally awakened with the intent to remain awake. The event marker allowed for prospective determination of bedtime and morning awakening times, rather than rely on participants' retrospective report of these events.

The actigraph measures activity levels and assigns a score corresponding to the amount of movement at 30-second intervals (or epochs). Each epoch is scored as “sleep” or “wake”, depending on a threshold setting (high, medium, or low) designated by the researcher. Kushida et al, (2001) indicate that the high threshold setting for actiwatch analysis yields the highest sensitivity, with specificity and accuracy comparable to other studies16. In this study, a high threshold (activity value = 80) was used. An epoch is rated as sleep or wake according to the following equation:

16 According to Kushida, sensitivity and specificity are defined as follows: Sensitivity (the ability to detect sleep via actigraphy when polysomnography scores it as sleep) = number of sleep epochs scored as sleep by actigraph and PSG / number of PSG-scored sleep epochs. Specificity (the ability to detect wake via actigraphy when polysomnography scores it as wake)= number of wake epochs scored as awake by actigraph and PSG / number of PSG-scored wake epochs. (Kushida et al., 2001).
(Mean activity score in epochs)(constant 0.888)
sampling length in minutes

If the value is less than or equal to the threshold (80), the epoch is scored as sleep. If the value is greater than the threshold, the epoch is scored as awake.

Sleep analysis software automatically calculated the following sleep indices: (1) Sleep onset latency = the period between bedtime and sleep onset as indicated by inactivity, (2) Actual sleep time = the amount of time between sleep onset and sleep end that is actually scored as sleep, and (3) sleep efficiency = Actual sleep time/Time in bed, (Mini Mitter Co., 2004).

Wrist actigraphy for the detection of sleep/wake states has been generally accepted as a useful research instrument, particularly in a multimethod assessment strategy, and more recently has been supported in the assessment of sleep disorders by the Standards and Practice Committee of the American Sleep Disorders Association (American Sleep Disorders Association, 1995). It is a cost-effective and less intrusive way to gain information about sleep patterns compared to polysomnography. This method of assessment has been used in both healthy and clinical populations, including HIV infected women (Bopp et al., 2004; Lee et al., 2001; Phillips & Skelton, 2001) and community studies of older adults (Ensrud et al., 2009; Loerbroks, Debling, Amelang & Sturmer, 2010; van den Berg et al., 2009).

Validation studies with wrist actigraphy most often compare actigraph derived sleep indices to polysomnography, considered to be the gold standard for measuring sleep states. A review of validation studies reported that correlations between actigraphy and polysomnography ranged from .72 to .98 for total sleep time, .56 to .91 for sleep efficiency, and .49 to .87 for wake after sleep onset (Tyron, 1996). In two studies
Sleep and psychomotor slowing in older HIV

comparing the Mini Mitter actiwatch with polysomnography, sensitivity, specificity, and accuracy rates were 0.92/0.95, 0.48/0.36, and 0.77/0.8 respectively (Babin, Lee, Halko, Boudreau, & George, 1997; Kushida et al., 2001).

Discrepancies between actigraph and polysomnographic readings are generally systematic and occur to a greater extent in patients with insomnia compared to good sleepers (Hauri & Wisbey, 1992; Tyron, 2004). Specifically, actigraphy tends to underestimate sleep onset and overestimate total sleep time in individuals with insomnia. Sleep onset estimation may be problematic with wrist actigraphy for participants with sleep onset insomnia, who may lie still for an extended period of time before falling asleep. For example, Hauri (1999) reported a mean actigraph sleep onset time of 5.5 min (SD = 6.2) vs. polysomnography sleep onset mean time of 34.2 (SD = 33.3) in a sample of 19 insomnia patients. Tyron (2004) argued that sleep onset is not a discrete event, and that actigraphy measures sleep onset at an earlier stage (loss of movement) than polysomnography (loss of movement and inability to hold an object). In a study of 36 participants with serious complaints of insomnia, Hauri & Wisbey (1992) reported a mean discrepancy between actigraphy and polysomnography of 49 minutes for total sleep time. However, in the same study, discrepancies were significantly larger when comparing sleep logs to polysomnography vs. actigraphy for some types of insomnia (i.e., insomnia associated with mental disorder, psychophysiological insomnia). In a pilot study using the Mini Mitter Actiwatch, participants with insomnia (N = 38, mean age 58.6 years) showed no significant differences in sleep onset scores, while total sleep time was significantly greater for the actigraph reading compared to polysomnography (377.4
Sleep and psychomotor slowing in older HIV

[SD = 77.3] min vs. 332.1 [SD = 81.5] min) (Edinger, Means, Stechuchak, & Olsen, 2004).

Sleep diary. Participants completed a daily sleep diary (See Appendix A) each morning during the time they wore the actiwatch. Subjective estimates of sleep indices are recommended as a useful adjunct to actigraphic data (Kushida et al., 2001). In addition, subjective estimates of sleep have been shown to correlate with cognitive decline in older adults, and may correlate to a greater degree than objectively measured sleep (Jelicic et al., 2002; Vitiello, Larsen, & Moe, 2004).

Participants were instructed to keep a sleep diary during the time they wore the wrist actigraph. Participants recorded the time they went to bed, perceived sleep onset, number and length of awakenings, and subjective report of sleep quality. In a sample of participants with a range of sleep disorders, Kushida et al., (2001) reported that sleep diary measures were not significantly different from polysomnography on total sleep time (5.9 ± 1.8 hrs for sleep diary vs. 5.5 ± 1.5), or sleep efficiency (73.9 % ± 19.2 for sleep diary vs. 68.4% ± 18.6), but sleep diaries reported significantly fewer awakenings per night (3.4 ± 3.5 vs. 33.1 ± 20). While reliability and validity are adequate, individuals with insomnia demonstrate consistent differences in their estimation of sleep onset latency and sleep duration compared to polysomnographic measures (Coates et al., 1983).

The limited number of days participants are asked to complete sleep diaries reflects concerns with recruitment and adherence with the self-monitoring protocol17. At

17 Although recommendations have been to maintain a sleep diary for at least 2 weeks to reduce reactivity (e.g., Morin, 1993), this study required participants to complete a diary for duration of time they wore the actiwatch. After consulting with the Hawaii Aging
least one study demonstrated high agreement between polysomnography and sleep diary after just a single night of recording. The correlation between measures from sleep diaries and polysomnography was .92 for a group of good sleepers (N = 25), and .85 for a group of narcoleptic participants (N = 25) (Rogers, Caruso, & Aldrich, 1993).

*The Pittsburgh Sleep Quality Index (PSQI).* The PSQI is a rationally derived, self-report scale developed to measure sleep quality in clinical populations (see Appendix B) (Buysee et al., 1989). The 19 item scale evaluates sleep over the past month, and yields a single global sleep score, in addition to generating scores for seven components of sleep; subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction (See Appendix C for scoring instructions). Evaluation of psychometric properties was carried out with three groups of participants, good sleepers (N = 52), poor sleepers (N = 34) diagnosed with major depressive disorder\(^\text{18}\), and poor sleepers that had been diagnosed with Disorder Initiating and Maintaining Sleep (DIMS; N = 45) or Disorders of Excessive Somnolence (DOES; N = 17) (Buysee et al., 1989). When component scores were

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\(^{18}\) Depression was assessed with the Schedule for Affective Disorders and Schizophrenia-Lifetime version (SADS-L; Endicott & Spitzer, 1978), and diagnosed according to Research Diagnostic Criteria (Spitzer et al., 1978; cited in Buysee, et al., 1989). Sleep disorder patients were diagnosed according to Association of Sleep Disorders Center (ASDC) criteria (ASDC, 1979; cited in Buysee, et al., 1989).
compared to the global PSQI score, the mean correlation coefficient was 0.58, with a range of 0.35 (sleep disturbances) to 0.76 (habitual sleep efficiency and subjective sleep quality). Test-retest reliability (N = 91) for the global PSQI score was 0.85 (p < 0.001), and for component scores ranged from 0.65 (p < 0.001) for medication use to 0.84 (p < 0.001) for sleep latency. Buysse, et al., (1989) assessed discriminative validity, and found that mean global PSQI scores differed significantly between all 3 subject groups, using an ANCOVA with age and sex as covariates. Using a global cut off score of 5 (> 5 constitutes poorer sleep quality), Buysse, et al., (1989) were able to correctly identify 88.5% of all control and poor sleeper participants, with a resulting sensitivity of 89.6% and specificity of 86.5%.

**Psychomotor performance**

*Aggregate measure of psychomotor performance.* The main cognitive criterion variable is an aggregate measure of z-score transformed measures of the psychomotor tests (NPZ3) derived from the neuropsychological test battery (i.e., the Grooved Pegboard, non-dominant administration, Wechsler Adult Intelligence Scale-Revised Digit Symbol, and Trail Making Test, Part B). The Hawaii Aging with HIV study was designed with significant input from researchers working with the Multicenter AIDS Cohort Study (MACS), a longitudinal study of HIV started in 1986. This prospective study included a neuropsychological component. The NPZ3 made up the psychomotor battery for the MACS cohort, and was developed rationally based on the best research evidence at the time. Use of a similar NPZ3 profile for the memory study was recommended as it allows for comparison across study groups of HIV patients. Norm-referenced Z-scores of the Grooved Pegboard, non-dominant administration, Wechsler
Adult Intelligence Scale-Revised (WAIS-R)-Digit Symbol, and Trail Making Test, Part B were averaged to construct a composite NPZ3 score measure of psychomotor performance.

**Grooved Pegboard, non-dominant administration.** The Grooved Pegboard test is a test of manual dexterity and complex coordination. It consists of a board containing a 5 X 5 set of slotted holes with grooves angled at varied directions. Participants are asked to place pegs in the holes using one hand, requiring rotation of each peg as it to allow for correct placement. The task is timed to completion (Lezak, Howieson, & Loring, 2004).

Practice effects have been reported with the Grooved Pegboard (e.g., Schmidt, Oliveira, Rocha, & Abreu-Villaca, 2000), although the effects are not consistent across studies. In a study of 605 healthy male participants (mean age 39.5), authors found test-retest correlation of .73 on the grooved pegboard, non-dominant hand. Cohen’s $d$ was .25 (Levine, Miller, Becker, Selnes, & Cohen, 2004). Dikman et al, (1999) found higher test-retest reliability (.86), with smaller effects for practice. Of the studies cited in Lezak (2004), 2 of the 3 noted small but significant differences between men and women with the non-dominant hand, with women performing slightly faster. In the third study, gender differences were not significant for the non-dominant hand. Across studies, the scores for the non-dominant hand showed less discrepancy between gender than dominant hand scores (Lezak, Howieson, & Loring, 2004; Schmidt, Oliveira, Rocha, & Abreu-Villaca, 2000).

The grooved pegboard is sensitive to neurologic changes and has been used in the detection and classification of lateralized or diffuse brain damage. For example, a prospective study reported that a performance deficit in the grooved pegboard (defined as
Sleep and psychomotor slowing in older HIV

at least 1 SD below norms) was predictive of a later diagnosis of HIV dementia (Hazard Ratio 2.24; 95% CI = 1.23 – 4.07 $p < .008$) (Stern et al., 2001).

*Wechsler Adult Intelligence Scale-Revised (WAIS-R), Digit Symbol Test.* The digit symbol is a test of psychomotor performance. It consists of 5 rows of small blank squares, each paired with a randomly generated number from 1 to 7 (total of 93 test items, plus 7 practice items). Participants are asked to fill in the blank squares with the symbol that is paired to the number above the space, completing as many as possible in a 90 second period. The score is the number of squares filled in correctly (Wechsler, 1981).

The Digit Symbol test is relatively unaffected by learning effects, but may be significantly affected by age. Motor persistence, response speed, sustained attention, and visuo-motor coordination contribute significantly to performance (Lezak et al., 2004). A meta-analysis of 141 studies reported that age accounted for 86% of the variance in a regression model using age, education, and year submitted as predictors of Digit Symbol scores (Hoyer, Stawski, Wasylyshyn, & Verhaeghen, 2004). In a study using symbol copy, paired recall, and free recall tasks to differentiate between speed, memory and incidental learning components of digit symbol, investigators reported that age accounted for nearly 50% of the variance in a WAIS-III Digit Symbol, while accounting for 40-45% of the variance in a symbol copy task (Joy, Kaplan, & Fein, 2004). Authors concluded that processing speed accounts for a significant portion of score reduction as individuals' age, but other factors such as memory changes are likely involved.

The measures from the Digit Symbol test have been shown to be reliable and highly sensitive to brain damage and cognitive decline, such as that associated with
dementia (Lezak et al., 2004). In reporting reliability, two studies of participants (age 25-54), testing 1 to 7 weeks apart, found correlation coefficients ranged from .82 to .89 (Matarazzo & Herman, 1984; Wechsler, 1981). In a study examining the relation between Digit symbol scores and dementia, Stern et al, (2001) reported participants (N = 146 with a decline in Digit Symbol Scores (> 1SD below norm) were almost 3 times as likely to develop dementia (Odds Ratio = 2.8; 95% CI= 1.49-5.28; p > .002).

*Trail Making Test (TMT); Part B.* The TMT is a test of complex visual scanning with a strong component of motor speed and agility. The participant is asked to draw a line to consecutively connect alternating circled numbers and letters. The test is timed and participants are urged to go as quickly as possible without lifting the pencil from the paper (Lezak et al., 2004). Participants in this study were allotted up to 180 seconds to complete that task, and the score given was the number of seconds taken to complete the task (Hawaii Aging with HIV- Manual of Operations).

Test-retest reliability coefficients vary, depending on the population used, with most above .6 (Lezak et al., 2004). For example, a study of 344 men (mean age = 41, 16 years education) reported a reliability of 0.70 with a mean interval between tests = 235 (SD= 127) days, with an Cohen’s d (a measure of effect size) .24 (Levine et al., 2004).

The TMT is sensitive to progressive cognitive decline and has been reported to be highly correlated with measures of daily function in older patients and in moderately to severely injured head trauma patients (Lezak et al., 2004). For example, in 50 elderly community and nursing home patients (age range = 63-89), Bell-McGinty and colleagues (2002) reported the TMT; part B was a significant predictor of the patient’s ability to
function in activities of daily living ($B = -0.45; t = -2.93; p < .00$) (Lezak et al., 2004; Bell-McGinty, Podell, Franzen, Baird, & Williams, 2002).

**Beck Depression Inventory**

The Beck Depression Inventory (BDI) is a widely used 21 item self-report scale that measures depressive symptoms (Beck, Rush, Shaw, & Emery, 1979; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). The BDI has demonstrated high reliability and validity. In a meta-analytic study of the BDI, Beck, Steer, & Garbin (1988), reported a mean coefficient alpha of 0.86 in psychiatric populations, and high correlations with other measures of depression. In studies with older adults, the BDI also demonstrated adequate reliability a group of community volunteers ($N = 82$, mean age $= 69.9$, SD $= 4.1$) with test-retest reliability of .86, and .76 reported for the mean coefficient alpha (Gallagher, Nies, & Thompson, 1982). Olin et al. (1992), reported the Beck Depression Inventory was found to have high sensitivity (100%) and specificity (96%) when using the score to differentiate between participants diagnosed with major depressive disorder and non-depressed controls in an older adult population ($N = 50$, mean age $= 64.2$, SD $= 5.4$). In addition, the authors also reported a high correlation between the Beck Depression Inventory and Geriatric Depression Scale ($r = .91, p < .01$) (Olin, Schneider, Eaton, Zemansky, & Pollock, 1992).

**Data management**

All data were double entered by research assistants, under the supervision of the co-PI (kf). Data were entered using excel for sleep data, and Microsoft Access for demographic, medical, and neuropsychological variables. Discrepancies between first
and second entries were resolved by referencing the original hard copies of the data
collection forms. All data were checked for completeness, plausibility, and logical
consistency. In approximately 90% of the data, the first and second entries were done by
different people. Analyses were done using the SAS (SAS Institute, Inc., Cary, NC) and
SPSS (SPSS Inc., Chicago, IL) v16.0 for Mac statistical packages.

Missing Data

The following sleep data were missing from the analysis: (a) For the actigraph
recordings, no data were missing from the second or third night recordings, (b) For the
Pittsburgh Sleep Quality Index, one participant did not complete several of the questions
on the form, and their global score could not be calculated, and (c) For the Sleep Diary, 8
participants did not fully complete both the second and third night diaries; six of the 8 did
not give information regarding how long they were awake when awakened during the
night, 4 did not provide sleep onset latency times, and 5 did not provide either sleep bed
time or awakening times for one or both of the nights used in data analysis. In such
cases, only the variables that included both the second and third night scores were
included in the analysis. Neuropsychological scores (WAIS-R Digit Symbol, Grooved
Pegboard, non-dominant, and Trail Making Test, Part B) were available for all
participants with no missing data.
CHAPTER 3

Results

Study Goal 1: Descriptive Statistics

Sleep Data. Table 2 includes means and standard deviation scores for Sleep Data. For the actigraph and sleep diary scores, data provided are mean values for the second and third nights of recording.

The HIV positive older group reported a higher proportion of disturbed sleep (as defined by a global Pittsburg Sleep Quality Index score of greater than 5) than reported by the control groups in the study, or compared to studies with non-clinical participants. In the HIV positive older group, 27 of the 38 participants (71%) had global Pittsburg Sleep Quality scores in the sleep disturbed range, compared to 12 of 31 participants (39%) in the older HIV negative group and 6 of 15 participants (40%) in the younger HIV positive group. Studies of non-clinical community groups report lower rates of disturbed sleep similar to the control groups. For example, a non-clinical sample of 112 community volunteers reported only 34.5% had disturbed sleep as defined by the PSQI (Grandner, Kripke, Yoon, & Youngstedt, 2006).
Table 2: Mean Scores and Standard Deviation Scores for Sleep Questionnaires

<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>HIV pos (50+ yrs)</th>
<th>HIV neg (50+ yrs)</th>
<th>HIV pos (20-40yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Actigraph: Total Sleep (min)</td>
<td>394.1</td>
<td>89.0</td>
<td>380.7</td>
</tr>
<tr>
<td>Actigraph: Sleep Onset Latency (min)</td>
<td>25.1</td>
<td>43.9</td>
<td>14.6</td>
</tr>
<tr>
<td>Actigraph: Sleep Efficiency (%)</td>
<td>82.5</td>
<td>11.2</td>
<td>86.8</td>
</tr>
<tr>
<td>Pittsburgh Sleep Quality Index (PSQI) Global Score</td>
<td>7.6*</td>
<td>3.6</td>
<td>4.5*</td>
</tr>
<tr>
<td>Sleep Diary: Total Sleep (min)</td>
<td>370.8</td>
<td>109.7</td>
<td>376.3</td>
</tr>
<tr>
<td>Sleep Diary: Sleep Onset Latency (min)</td>
<td>35.0</td>
<td>47.9</td>
<td>16.4</td>
</tr>
<tr>
<td>Sleep Diary: Sleep Efficiency (%)</td>
<td>84.5</td>
<td>12.9</td>
<td>91.9</td>
</tr>
<tr>
<td>Sleep Diary: Wake after Sleep Onset (# times/night)</td>
<td>2.4</td>
<td>1.5</td>
<td>2.1</td>
</tr>
<tr>
<td>Sleep Diary: Wake after Sleep Onset (total min/night)</td>
<td>31.8</td>
<td>32.6</td>
<td>25.9</td>
</tr>
<tr>
<td>Sleep Diary: Daytime naps: (min)</td>
<td>28.1</td>
<td>40.5</td>
<td>28.1</td>
</tr>
<tr>
<td>Sleep Diary: Sleep Quality Score (^{b})</td>
<td>3.0**</td>
<td>0.9</td>
<td>3.5**</td>
</tr>
</tbody>
</table>

Note: Means for Actigraph and Sleep Diary are based on the means of the 2\(^{nd}\) and 3\(^{rd}\) nights of sleep assessed.

a. PSQI Global Score Range = 0-21; Scores above 5 are considered Sleep Disturbed (Buysee, Reynolds, Monk, Berman, & Kupfer, 1989).

b. Lickert Score range 1-5
*The older HIV positive group, compared to older HIV negative group scores are significantly different (p > .05)

**The older HIV positive group, compared to older HIV negative group scores are significantly different (p > .01)

Comparisons between the older HIV positive group and younger HIV positive group scores yielded no significant differences.
Study Goal 2: Between Group Analyses of Sleep Dimensions. The goal of the next set of analyses was to compare sleep dimensions of older HIV positive adults to those of younger HIV positive adults and older HIV negative adults. MANOVA’s were conducted in two separate analyses to facilitate comparison of the main study group (older HIV positive adults) with each of the respective control groups (older HIV negative group and younger HIV positive group). Analysis of group differences between the two control groups was not a focus of this study, therefore a three-way MANOVA was not indicated.

Comparison of older HIV positive group vs. the older HIV negative group. A one-way between groups multivariate analysis of variance (MANOVA) was conducted to examine group differences between the older HIV positive group and the older HIV negative control group on the following dependent measures of sleep: (a) sleep efficiency, sleep onset latency and total time asleep, as recorded by sleep Actigraph, (b) sleep efficiency, sleep onset latency, total time asleep, number of awakenings during the night, total time awake between sleep onset and final awakening, total time napping, and subjective sleep quality as reported by the sleep diary and (c) the global score for the Pittsburgh Sleep Quality Index.

There was a statistically significant difference between the older HIV positive group and older HIV negative group on combined dependent variables (F[9,62] 2.63; p < 0.01; Wilks’ Lambda = .664; partial eta squared = .34). When the results for the dependent variables were considered separately, the only differences to reach statistical significance, using a Bonferroni adjusted alpha level of 0.0045, were PSQI Global scores (F[1,61] 15.19; p < 0.00; partial eta squared = .199) and subjective report of sleep quality
taken from the sleep diary (F[1,61] 9.16; p < 0.04; partial eta squared = .131). An inspection of the mean scores indicated that the older HIV positive group reported significantly poorer sleep quality than the older HIV negative comparison group as reported by both the PSQI global score (M = 7.6, SD = 3.6 for HIV positive vs. M = 4.4, SD = 2.8 for HIV negative), and the sleep diary (M = 2.9, SD = 0.84 for HIV positive vs. M = 3.5, SD = .74 for HIV negative).

Comparison of older HIV positive group vs. the younger HIV positive group. A one-way between-groups multivariate analysis of variance (MANOVA) was also conducted to examine group differences between the older HIV positive group and the younger HIV positive control group on the same sleep measures listed above. There was a no statistically significant difference between the older HIV positive group and younger HIV positive group on combined dependent variables (F[9,47] 1.29; p < 0.274).

Comparison of Actigraph and Sleep Diary Measures. The three groups of participants demonstrated varying degrees of differences between actigraph data vs. sleep diary data. In the older HIV positive group, discrepancies between actigraph and sleep diary report were greatest for sleep efficiency, and most congruent for estimates of sleep onset latency. For example, for sleep onset latency, 23.7 % of older HIV positive group recorded a sleep onset latency of greater than 30 minutes via actigraph vs. 33.3 % for sleep diary. In the comparison groups, 12.9 % of the older HIV negative group recorded a sleep onset latency of greater than 30 minutes via actigraph vs. 13.8 % for sleep diary, and 25 % of the younger HIV positive group recorded a sleep onset latency of greater than 30 minutes via actigraph vs. 18.8 % for sleep diary.
All groups subjectively over-estimated sleep efficiency when compared with actigraph measures. For example, 50.0% of older HIV positive group recorded a sleep efficiency of 85% or greater via actigraph vs. 67.6% for sleep diary. Similarly, 64.5% of the older HIV negative group recorded a sleep efficiency of 85% or greater via actigraph vs. 93.1% for sleep diary, and 43.8% of the younger HIV positive group recorded a sleep efficiency of 85% or greater via actigraph vs. 80.0% for sleep diary.

Aggregation of sleep indices

Table 3 reports Pearson product-moment correlation coefficients among sleep indices, used to determine suitability of aggregating sleep measures (i.e., correlations > 0.5). Among the five variables considered for aggregation (Actigraph SOL and Sleep efficiency, Sleep Diary SOL and Sleep efficiency, and PSQI global score), the SOL and sleep efficiency scores for the actigraph were suitable for aggregating together (0-.76, p>.01). Similarly, SOL and sleep efficiency scores for the sleep diary were sufficiently correlated to aggregate (0-.81, p>.01). In examining the PSQI global score compared to actigraph and sleep diary measures, the actigraph scores were not sufficiently correlated, and did not meet criteria to form an aggregated score (.22 & -.27), while correlations with the sleep diary met criteria for sleep efficiency (-.54), but not for SOL (.45). Finally, Actigraph scores were sufficiently correlated with Sleep Diary SOL (.56 & -.51) to justify aggregation, but not Sleep Diary Sleep Efficiency (-.43 & .47). The strongest correlations occur between sleep indices of the same type of measure rather than specific sleep variables across measures. Therefore, sleep scores were aggregated as follows,(1) Actigraph SOL and Actigraph Sleep Efficiency, (2) Sleep Diary SOL and Sleep Diary Sleep Efficiency, and (3) PSQI global score.
### Table 3: Intercorrelations between Subjective and Objective Sleep Measures.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>N</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Actigraph: Total Sleep (min)</td>
<td>85</td>
<td>--</td>
<td>-.25*</td>
<td>.37**</td>
<td>-.03</td>
<td>.42**</td>
<td>-.16</td>
<td>.11</td>
<td>.21</td>
<td>.14</td>
<td>.07</td>
</tr>
<tr>
<td>2) Actigraph: SOL (min)</td>
<td>85</td>
<td>--</td>
<td>-.76**</td>
<td>.22*</td>
<td>-.06</td>
<td>.56**</td>
<td>-.43**</td>
<td>-.04</td>
<td>.02</td>
<td>-.32**</td>
<td></td>
</tr>
<tr>
<td>3) Actigraph: Sleep Efficiency (%)</td>
<td>85</td>
<td>--</td>
<td>-.27*</td>
<td>.25*</td>
<td>-.51**</td>
<td>.47**</td>
<td>-.02</td>
<td>-.07</td>
<td>.35**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) PSQI: Global Score</td>
<td>84</td>
<td>--</td>
<td>-.16</td>
<td>.45**</td>
<td>-.54**</td>
<td>.11</td>
<td>.38**</td>
<td>-.42**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Sleep Diary: Total Sleep (min)</td>
<td>76</td>
<td>--</td>
<td>-.40**</td>
<td>.56**</td>
<td>.02</td>
<td>-.20</td>
<td>.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6) Sleep Diary: SOL (min)</td>
<td>81</td>
<td>--</td>
<td>-.81**</td>
<td>.05</td>
<td>.11</td>
<td>-.39**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7) Sleep Diary: Sleep Efficiency</td>
<td>78</td>
<td>--</td>
<td>-.15</td>
<td>-.54**</td>
<td>.54**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8) Sleep Diary: WASO (number times)</td>
<td>84</td>
<td>--</td>
<td>.32**</td>
<td>.36**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9) Sleep Diary: WASO (total mins)</td>
<td>79</td>
<td>--</td>
<td>.49**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10) Sleep Diary: Sleep Quality Score</td>
<td>85</td>
<td>--</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** Correlation is significant at the 0.01 level (2-tailed);  * Correlation is significant at the 0.05 level (2-tailed).

Abbrev. SOL = Sleep Onset Latency; PSQI = Pittsburgh Sleep Quality Index; WASO = Wake after Sleep Onset.
**Study Goals 3 & 4 The Incremental Contribution of Sleep Measures in Predicting variance in Psychomotor Performance, Above and Beyond that associated with Age, Depression, CD4, and Length of Infection.** Two sets of multiple regression analyses were conducted to examine the variance accounted for in the NPZ3 score by the aggregate scores of sleep quality, while controlling for age, length of infection, CD4, gender, education and depression. Table 4 reports Mean, Standard Deviations, and correlations among regression variables. Although inspection of Table 4 indicates that none of the independent variables appear to be related to the dependent variable (i.e., .3 or above), regression analyses were conducted to fulfill stated goals of the dissertation.

**Analysis 1:** A full regression model was constructed that included the NPZ3 score as the outcome variable, and sleep quality, age, length of infection, CD4, education, and depression scores as predictor variables.

\[ Y = \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + e \]  

where \( Y \) = NPZ3 score, \( \beta \) = weights for predictors, \( X_1 \) = aggregated Actigraph scores, \( X_2 \) = aggregated sleep diary scores, \( X_3 \) = PSQI global z-score, \( X_4 \) = age, \( X_5 \) = length of infection, \( X_6 \) = CD4, \( X_7 \) = education, \( X_8 \) = depression and \( e \) = error.

A restricted regression model was constructed with the sleep quality scores removed.

\[ Y = \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + e \]  

where \( Y \) = NPZ3 score, \( \beta \) = weights for predictors, \( X_4 \) = age, \( X_5 \) = length of infection, \( X_6 \) = CD4, \( X_7 \) = education, \( X_8 \) = depression, and \( e \) = error.

A comparison the \( R^2 \) of the restricted model with the \( R^2 \) of the full model was made, testing for the significance of the change in \( R^2 (\Delta R^2) \). Table 5 reports a summary of the
regression analysis. In the full model, sleep quality, age, length of infection, CD4, education, and depression in combination accounted for 11.0% of the variance in the NPZ3 score. In the restricted model, age, length of infection, CD4, education and depression accounted for 9.3% of the variance in NPZ3 score. According to the F test, there is no significant difference between the full and restricted models. Aggregated measures of sleep quality (in combination or alone) did not account for a significant amount of the variance in the NPZ3 score above and beyond age, length of infection, CD4, education, and depression.

**Analysis 2:** Stepwise multiple regression analyses were conducted to examine the variance accounted for in the NPZ3 score by the aggregate score of sleep quality, while controlling for age, length of infection, CD4, gender, education and depression. Using probability .05 to retain and .1 to remove a variable, a series of stepwise models were constructed. None of the variables entered were significant predictors of variance accounted for in the NPZ3 score.
### Table 4

Means, Standard Deviations, and Correlations Among Regression Variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Neuropsychological z-score aggregate</td>
<td>54</td>
<td>.37</td>
<td>.81</td>
<td>--</td>
<td>-.12</td>
<td>.06</td>
<td>.1</td>
<td>-.26*</td>
<td>-.14</td>
<td>-.11</td>
<td>-.03</td>
<td>-.00</td>
</tr>
<tr>
<td>2) Age (years)</td>
<td>54</td>
<td>51.7</td>
<td>11.2</td>
<td>--</td>
<td>.14</td>
<td>-.19</td>
<td>.06</td>
<td>.53**</td>
<td>.11</td>
<td>-.33**</td>
<td>.19</td>
<td></td>
</tr>
<tr>
<td>3) Education (years)</td>
<td>54</td>
<td>14.9</td>
<td>2.7</td>
<td>--</td>
<td>-.01</td>
<td>.06</td>
<td>.10</td>
<td>.09</td>
<td>-.23</td>
<td>.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) CD4 (cells/µL)</td>
<td>53</td>
<td>497.6</td>
<td>243.9</td>
<td>--</td>
<td>-.07</td>
<td>-.09</td>
<td>.17</td>
<td>.00</td>
<td>-.22*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Beck Depression Inventory</td>
<td>53</td>
<td>6.3</td>
<td>5.1</td>
<td>--</td>
<td>-.03</td>
<td>.45**</td>
<td>-.23</td>
<td>-.26*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6) Length of time HIV positive (years)</td>
<td>54</td>
<td>12.6</td>
<td>6.7</td>
<td>--</td>
<td>.08</td>
<td>-.21</td>
<td>.02</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7) Pittsburg Sleep Quality Index z-score</td>
<td>53</td>
<td>.28</td>
<td>1.0</td>
<td>--</td>
<td>-.27*</td>
<td>-.19</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>8) Sleep Diary z-score aggregate</td>
<td>49</td>
<td>-.07</td>
<td>.65</td>
<td>--</td>
<td></td>
<td>.23</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>9) Actigraph z-score aggregate</td>
<td>54</td>
<td>-.06</td>
<td>.72</td>
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<td></td>
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<td></td>
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</tr>
</tbody>
</table>

** Correlation is significant at the 0.05 level;  * Correlation is significant at the 0.01 level.
Sleep and psychomotor slowing in older HIV

Table 5: Summary of Regression Analysis (full and restricted models).

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SEB</th>
<th>β</th>
<th>*R²</th>
<th>F</th>
<th>R² Change</th>
<th>F comp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1 (restricted model)</td>
<td></td>
<td></td>
<td></td>
<td>.09</td>
<td>.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>-.01</td>
<td>.01</td>
<td>-.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td>-.03</td>
<td>.04</td>
<td>.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of time HIV + (years)</td>
<td>.01</td>
<td>.02</td>
<td>.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 (cells/µL)</td>
<td>.00</td>
<td>.00</td>
<td>.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>-.04</td>
<td>.02</td>
<td>.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2 (full model)</td>
<td></td>
<td></td>
<td></td>
<td>.11</td>
<td>.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>-.01</td>
<td>.01</td>
<td>-.16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (years)</td>
<td>.02</td>
<td>.05</td>
<td>.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of time HIV+ (years)</td>
<td>.01</td>
<td>.02</td>
<td>.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 (cells/µL)</td>
<td>.00</td>
<td>.00</td>
<td>.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>-.04</td>
<td>.03</td>
<td>-.26</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSQI Sleep Quality Index z-score</td>
<td>-.06</td>
<td>.14</td>
<td>-.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Diary z-score aggregate</td>
<td>-.17</td>
<td>.22</td>
<td>-.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Actigraph z-score aggregate</td>
<td>-.01</td>
<td>.19</td>
<td>-.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison of Model 1 and 2</td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
<td>.29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Sleep and psychomotor slowing in older HIV

Note: $R^2$ change = the difference between the $R^2$ of Model 1 and Model 2; $F_{\text{comp}}$ = the calculated F score when comparing Model 1 and Model 2; NPZ-PM= Neuropsychological z-scores- psychomotor, BDI= Beck Depression Inventory.

* $R^2$ is reported, adj $R^2$ is less than zero
CHAPTER 4

Discussion

This study sought to extend knowledge of sleep patterns in older adults living with HIV, and examine the relation between sleep quality and psychomotor function. While several studies in HIV have focused on sleep, this study extended previous work by providing both subjective and objectively measured data to estimate sleep indices for an older group of HIV positive adults, and by providing control groups of similar aged HIV negative and younger HIV positive participants. The few previous studies that have utilized multiple measures (i.e., actigraphy or polysomnography with self report), either focused on different target groups within the HIV population (i.e., Lee, Portillo, & Miramontes, 2001, Phillips, K & Skelton, W., 2001), have small sample sizes (e.g., Norman, et al, 1992; White et al., 1995), or have been limited by a lack of HIV negative control group (Reid & McGrath, 2007). The multiple measurement strategies in the present study can provide more precise information on sleep and how it is experienced in this population, improving clinicians ability to manage disturbed sleep in older adults with HIV.

Using the PSQI, estimates of disturbed sleep for both HIV positive groups can be compared across multiple previous studies and other populations. There was a high proportion (71%) of older HIV positive participants with PSQI scores in the sleep disturbed range in this study. This is congruent with previous HIV research (e.g., 61-73%; Cohen et al., 1996; Cruess et al., 2003; Nokes & Kendrew, 2001). In addition, rates of disturbed sleep for the older HIV positive group were significantly higher than reports of disturbed sleep in the general population (e.g., 30-32% in Austrian and Japanese
community studies), or healthy older adults (e.g., 16 to 33%), and more consistent with other studies of medically ill patients (e.g., 61% and 71% reported in breast cancer and hemodialysis patients respectively) (Doi, Minowa, Uchiyama, & M., 2001; Fortner, Stepanski, Wang, Kasprowicz, & Durrence, 2002; Iliescu et al., 2003; Zeitlhofer et al., 2000). The younger HIV positive group reported disturbed sleep in proportions similar to the HIV negative older group and other studies of healthy older adults.

When comparing the older HIV positive participants to the control groups, there were no significant differences in sleep indices across the three participant groups, or across methodologies, aside from self-reported sleep quality. For example, all three groups had similar mean total sleep times and sleep efficiencies, with total sleep times between 6 to 7 hrs/night, and mean sleep efficiency that ranged from 83% to 92%. In addition, all three groups reported being awakened from sleep an average of 2 times per night, and napped an average of 30 minutes or less during the day. The average sleep duration is consistent to other studies of sleep in outpatients with HIV, and is also comparable with reports of sleep duration in community studies reporting sleep for older adults (e.g, National Sleep Foundation, 2003; Girardin, Kripke, Ancoli-Israel, Klauber, & Sepulveda, 2000; Groeger, Zijllstra, & Dijk, 2004). For example, the average duration of sleep for the 2003 National Sleep Foundation study of older adults (aged 55 to 84 years) was 7.0 hours per night (NSF, 2003). Based on normative changes associated with age, it was expected that the older HIV positive group would report shorter total sleep times, longer time awake after sleep onset, and longer nap times, when compared to the younger HIV positive group (Vitiello, 2006). While trends towards these differences were observed, they were not statistically significant for this sample. One possible explanation
would be that the younger HIV positive group was reporting changes in sleep similar to those observed in healthy aging. Larger participant groups (particularly the younger HIV positive control group) would allow for more definitive conclusions.

For older HIV positive participants in this study, the perception of sleep quality does not appear to be related to duration of sleep or other sleep indices. While all the participant groups reported similar sleep durations/indices, the self-reported quality of sleep was significantly poorer for the older HIV positive group when compared to the age-matched HIV negative group. The most likely explanation for this finding is that some symptoms commonly associated with a diagnosis of HIV (i.e., depression, anxiety, pain, fatigue) are more likely to contribute to sleep quality than changes in sleep associated with age or HIV per se. For example, neuropathy can be painful and has been reported in significant proportions of HIV patients. Recent research also indicated this condition is disproportionately higher (e.g., 20% vs 50%) in older than in younger HIV positive patients (Watters, 2004). Also, while study criteria excluded participants with significant depressive symptoms (i.e., BDI scores over 22), 15% of the entire participant group, and 19% of the older HIV participants had BDI scores over 10, indicating they could be mildly to moderately depressed. In addition, some of the medications for treatment of HIV are associated with changes in sleep patterns and could affect quality of sleep. For example, efavirenz, a non-nucleoside reverse transcriptase inhibitor (NNRTI) used as part of highly active antiretroviral therapy (HAART) for the treatment of HIV, is known to increase incidence of insomnia and/or nightmares.

Examining the total participant group (N = 85), actigraph and sleep diary scores were moderately correlated with each other for measures of sleep onset, sleep efficiency,
and total sleep time. The sleep onset latency and sleep efficiency scores for the sleep diary were also moderately correlated with the PSQI global score. However, actigraph measures of sleep onset and sleep efficiency were only weakly correlated to the PSQI (i.e., .22 to .27), and there was no significant correlation between the PSQI global score and estimates of total sleep time as measured objectively by actigraph, or by subjective report. As expected, self report measures (i.e., sleep diary and PSQI) were more strongly correlated with each other than the actigraph measures, and the PSQI demonstrated variability in how it correlated with the other sleep measures.

There are several possible explanations to account for the lack of correlation between PSQI global scores and actigraph or sleep diary estimates of total sleep time, and low correlations with other sleep indices. For example, the total sleep time is calculated based on several sleep indices (SOL, time awake after sleep onset, time awakened in the morning), each only weakly correlated with the PSQI. In addition, the PSQI is an estimate of typical sleep over the past month, rather than a daily accounting of sleep, and therefore more vulnerable to bias than the sleep diary or actigraph. It may be particularly vulnerable to negative bias (i.e., more indicators of poor sleep) if the participants’ are also reporting symptoms of depression. Finally, the PSQI takes several other markers of health and well being into account when calculating overall sleep quality (e.g., pain, problems breathing, coughing/snoring, or feeling hot/cold), which could significantly affect report of sleep quality.

This study did not find that variation in sleep indices was significantly associated with variation in psychomotor scores as has been reported in some studies of older HIV negative adults. One factor that confounds the ability to draw conclusions about the lack
of association is the wide degree of variation across studies in the measures used to evaluate psychomotor function (e.g., single test, aggregate of multiple tests) and in the assessment strategies employed for estimating sleep indices (e.g., single nights, across several nights, etc.). Sleep disturbances in particular, have a great degree of variation in the way they are measured and defined across studies. While some previous research has found an association between sleep and cognitive and/or psychomotor impairment, several other studies reported no association.

There are several limitations to this study. First, while sample size of the older HIV positive and negative groups was adequate for descriptive analyses, it was small for sufficient power when conducting multiple analyses as in the MANOVA and regression analysis. As mentioned earlier, the size of the younger HIV positive group was particularly small, reducing the ability to detect significant differences between groups. Second, the number of days the sleep diaries were completed was less than is recommended in guidelines for research, and study participants did not have several days to acclimate keeping a sleep diary. As a result, sleep patterns may have been affected to some degree by reactivity associated with keeping track of sleep. This affect was reduced by discounting the first night’s data for sleep. Third, the study did not restrict data collection or distinguish between data collected during the week vs. weekends to minimize variability in sleep patterns. In this study, restricting the days available for study would have resulted in significant delays in obtaining data. While differentiation between weekday and weekends is a recommended research protocol, recent evidence suggests that the difference between weekday/weekend sleep patterns may not be significant, particularly in the older participant groups, whose sleep is less likely to be
affected by work schedules. Finally, some factors likely to contribute to sleep
disturbance and/or psychomotor function were not addressed in this study, such as the use
of medications and chronic pain conditions. The age and HIV status of the participants
increased the likelihood of participants taking medications that may affect sleep
(purposefully or as a side effect). For example, as mentioned earlier, HIV positive
participants in particular were often taking multiple medications as part of their HAART
regime, some of which are known to affect sleep as a possible side effect.

Future studies could focus on continuing to delineate sleep difficulties in older
HIV positive adults and ways to address them to improve quality of life for HIV patients.
For example, three days is a minimally acceptable period to examine sleep patterns in
research participants. Actiwatch readings and sleep diaries kept over a longer period (e.g.
2 weeks) would provide more data on specific sleep variables and patterns. In addition,
more exploration of plausible causative factors for disturbed sleep (e.g., medications,
medical condition related to HIV such as neuropathy, age) could improve treatment
possibilities for patients with HIV. Finally, future studies should address the efficacy of
current sleep therapies (e.g., medication, cognitive-behavioral treatment, sleep restriction,
etc). To date, there are few studies that attempt to improve sleep quality by addressing
sleep hygiene (e.g, Hudson, Portillo, & Lee, 2008), or other likely causes (e.g.,
depression, anxiety, pain) of poor sleep.
Sleep and psychomotor slowing in older HIV

References


Bell-McGinty, S., Podell, K., Franzen, M., Baird, A. D., & Williams, M. J. (2002). Standard measures of executive function in predicting instrumental activities of


Sleep and psychomotor slowing in older HIV


Sleep and psychomotor slowing in older HIV


<table>
<thead>
<tr>
<th>SLEEP DIARY</th>
<th>Example</th>
<th>Morning 1</th>
<th>Morning 2</th>
<th>Morning 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Yesterday, I napped from _____ to _____ (note the times of all naps).</td>
<td>1:50 to 2:30 pm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Yesterday, I took ____mg of medication and/or ____oz of ____ as a sleep aid.</td>
<td>Ambien 5 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Last night, I went to bed and turned the lights off at ____ o’clock.</td>
<td>11:15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. After turning the lights out, I fell asleep in ____ minutes.</td>
<td>40 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. My sleep was interrupted ____ times (specify the number of nighttime awakenings).</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. My sleep was interrupted for ____ minutes (specify the duration of each awakening).</td>
<td>10 5 45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. This morning, I woke up at ____ o’clock (note the time of the last awakening).</td>
<td>6:15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. This morning, I got out of bed at ____ o’clock (specify the time).</td>
<td>6:40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. When I got up this morning I felt _____. (1 = exhausted, 5 = very well rested)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Overall, my sleep last night was ____. (1 = very poor, 5 = very good)</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INSTRUCTIONS
In order to better understand your sleep, we would like you to collect some important information on your sleep pattern. After you get up in the morning, please answer all 10 questions on the sleep diary. It is important that you complete this diary every morning. For example, after your first night of wearing the actigraph, complete the column under morning 1, the next night, complete the column under morning 2, and so forth. It is difficult to estimate how long you take to fall asleep at night or how long you are awake at night. Please remember, however, that we only want your best estimates. If there should be some unusual event on a given night (e.g., illness, emergency, phone call) please make a note of it. Below are some guidelines to help you answer each question. An example is also provided on the diary.

1. Napping: This should include all naps even if they were not intentional. For instance, if you dozed off in front of the TV for 10 minutes, please write it down. Please include AM or PM.
2. Sleep Aid: You should include both prescribed and over-the-counter medications, as well as alcohol used specifically to help you get to sleep.
3. Bedtime: This is the time you go to bed and actually turn the lights off. If you go to bed at 10:45 but turn the lights off at 11:15, you should write both times in that space.
4. Sleep-onset latency: Provide your best estimate of how long it took you to fall asleep after you turned the lights off and intended to go to sleep.
5. Number of Awakenings: This is the number of times you remember waking up during the night.
6. Duration of Awakenings: Please estimate to the best of your knowledge how many minutes you spent awake for each awakening. If this proved impossible, then just estimate the number of minutes you spent awake for all awakenings combined. This should not include your last awakening in the morning, as this will be logged in number 7.
7. Morning awakening: This is the very last time you woke up in the morning. If you woke up at 4:00 am and never went back to sleep, this is the time to record. However, if you woke up at 4:00 am but went back to sleep for a brief time (e.g., 6:00 am to 6:20 am), then your last awakening would be 6:20 am.
8. Out-of-bed: This is the time you actually got out of bed for the day.
9. Feeling upon arising: Please use the following 5-point scale:
   1 = exhausted, 2 = tired, 3 = average, 4 = rested, 5 = very well rested.
10. Sleep Quality:
    1 = very poor, 2 = poor, 3 = average quality, 4 = good, 5 = very good.

Appendix B: Pittsburg Sleep Quality Index (PSQI)

Instructions:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed at night?
   USUAL BED TIME ______________

2. During the past month, how long (in minutes) does it usually take you to fall asleep each night?
   NUMBER OF MINUTES ______________

3. During the past month, when have you usually gotten up in the morning?
   USUAL GETTING UP TIME ______________

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)
   HOURS OF SLEEP PER NIGHT ______________

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you….
   (a) Cannot get to sleep within 30 minutes
       Not during the past month ___  Less than once a week ___  Once or twice a week ___  Three or more times a week ___

   (b) Wake up in the middle of the night or early morning
       Not during the past month ___  Less than once a week ___  Once or twice a week ___  Three or more times a week ___

   (c) Have to get up to use the bathroom
       Not during the past month ___  Less than once a week ___  Once or twice a week ___  Three or more times a week ___

   (d) Cannot breathe comfortably
       Not during the past month ___  Less than once a week ___  Once or twice a week ___  Three or more times a week ___

   (e) Cough or snore loudly
       Not during the past month ___  Less than once a week ___  Once or twice a week ___  Three or more times a week ___
(f) Feel too cold  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

(g) Feel too hot  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

(h) Had bad dreams  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

(i) Have pain  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

(j) Other reason(s), please describe ______________________________________
____________________________________________________________________
____________________________________________________________________

| How often during the past month have you had trouble sleeping because of this? |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Not during the past month ____ | Less than once a week ____ | Once or twice a week ____ | Three or more times a week ____ |

6. During the past month, how would you rate your sleep quality overall?  
Very good _____  
Fairly good _____  
Fairly bad _____  
Very bad _____

7. During the past month, how often have you taken medicine (prescribed or “over the counter”) to help you sleep?  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?  
Not during the past month ____  Less than once a week ____  Once or twice a week ____  Three or more times a week ____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?  
No problem at all _____  
Only a very slight problem _____  
Somewhat of a problem _____  
A very big problem _____

86
Appendix C: Scoring Instructions for the Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) contains 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). Only self-rated questions are included in the scoring. The 19 self-rated items are combined to form seven “component” scores, each of which has a range of 0-3 points. In all cases, a score of “0” indicates no difficulty, while a score of “3” indicates severe difficulty. The seven component scores are then added to yield one “global” score, with a range of 0-21 points, “0” indicating no difficulty and “21” indicating severe difficulties in all areas.

Scoring proceeds as follows:

**Component 1: Subjective sleep quality**

Examine question #6, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Component 1 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Very good”</td>
<td>0</td>
</tr>
<tr>
<td>“Fairly good”</td>
<td>1</td>
</tr>
<tr>
<td>“Fairly bad”</td>
<td>2</td>
</tr>
<tr>
<td>“Very Bad”</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 1 score: _______

**Component 2: Sleep latency**

Examine question #2, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 15 minutes</td>
<td>0</td>
</tr>
<tr>
<td>16-30 minutes</td>
<td>1</td>
</tr>
<tr>
<td>31-60 minutes</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 60 minutes</td>
<td>3</td>
</tr>
</tbody>
</table>

Question #2 score: _______

2) Examine question #5a, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td>0</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>1</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>2</td>
</tr>
<tr>
<td>Three or more times a week</td>
<td>3</td>
</tr>
</tbody>
</table>

Question #5a score: _______

3) Add #2 score and #5a score

4) Assign component 2 score as follows:

<table>
<thead>
<tr>
<th>Sum of #2 and 5a</th>
<th>Component 2 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>1</td>
</tr>
<tr>
<td>3-4</td>
<td>2</td>
</tr>
<tr>
<td>5-6</td>
<td>3</td>
</tr>
</tbody>
</table>
Sleep and psychomotor slowing in older HIV

Component 2 score: 

**Component 3: Sleep Duration**

Examine question #4, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Component 3 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 7 hours</td>
<td>0</td>
</tr>
<tr>
<td>6-7 hours</td>
<td>1</td>
</tr>
<tr>
<td>5-6 hours</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 5 hours</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 3 score: 

**Component 4: Habitual sleep efficiency**

1. Write the number of hours slept (question #4) here: _______
2. Calculate the number of hours spent in bed:
   - Getting up time (question #3): _______
   - Bedtime (question #1): _______
   - Number of hours spent in bed: _______
3. Calculate habitual sleep efficiency as follows:
   \[
   \left( \frac{\text{Number of hours slept}}{\text{Number of hours spent in bed}} \right) \times 100 = \text{Habitual sleep efficiency} \%
   \]
   \[
   \left( \frac{\text{_______}}{\text{_______}} \right) \times 100 = \text{_______ \%}
   \]
4. Assign component 4 score as follows:

<table>
<thead>
<tr>
<th>Habitual sleep efficiency %</th>
<th>Component 4 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 85%</td>
<td>0</td>
</tr>
<tr>
<td>75-84 %</td>
<td>1</td>
</tr>
<tr>
<td>65-74%</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 65%</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 4 score: 

**Component 5: Sleep disturbances**

1. Examine questions #5b – 5j, and assign scores for each question as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td>0</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>1</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>2</td>
</tr>
<tr>
<td>Three or more times a week</td>
<td>3</td>
</tr>
</tbody>
</table>

#5b score _______
e score _______
d score _______
e score _______
f score _______
g score _______
h score _______
i score _______
j score _______

(2) Add the score for questions # 5b- 5j:
Sum of # 5b- 5j: _______

(3) Assign component 5 score as follows:

<table>
<thead>
<tr>
<th>Sum of #5b- 5j</th>
<th>Component 5 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-9</td>
<td>1</td>
</tr>
<tr>
<td>10-18</td>
<td>2</td>
</tr>
<tr>
<td>19-27</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 5 score:_______

Component 6: Use of sleeping medication

(1) Examine question #7 and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Component 6 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not during the past month</td>
<td>0</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>1</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>2</td>
</tr>
<tr>
<td>Three or more times a week</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 6 score:

Component 7: Daytime dysfunction

(1) Examine question #8, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>0</td>
</tr>
<tr>
<td>Once or twice</td>
<td>1</td>
</tr>
<tr>
<td>Once or twice each week</td>
<td>2</td>
</tr>
<tr>
<td>Three or more times each week</td>
<td>3</td>
</tr>
</tbody>
</table>

Question #8 score: _______

(2) Examine question #9, and assign scores as follows:

<table>
<thead>
<tr>
<th>Response</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No problem at all</td>
<td>0</td>
</tr>
<tr>
<td>Only a very slight problem</td>
<td>1</td>
</tr>
<tr>
<td>Somewhat of a problem</td>
<td>2</td>
</tr>
<tr>
<td>A very big problem</td>
<td>3</td>
</tr>
</tbody>
</table>

Question #9 score: _______
(3) Add the scores for question #8 and #9:

Sum of #8 and #9: _______

(4) Assign component 7 score as follows:

<table>
<thead>
<tr>
<th>Sum of #8 and #9</th>
<th>Component 7 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>1</td>
</tr>
<tr>
<td>3-4</td>
<td>2</td>
</tr>
<tr>
<td>5-6</td>
<td>3</td>
</tr>
</tbody>
</table>

Component 7 score: _______

Global PSQI Score

Add the seven component scores together:

Global PSQI score: _______
Appendix D: Neuropsychological Battery for the Aging with HIV Study

1. North American Adult Reading Test (NAART)

2. Rey Auditory Verbal Learning Test (RAVLT)
   a. Trials 1 through 5
   b. Immediate Recall
   c. Delayed Recall

3. Rey Complex Figure Test (RCFT)
   a. Copy Trial
   b. Immediate Recall
   c. Delayed Recall

4. Wechsler Adult Intelligence Scale - Revised (WAIS-R)
   a. Digit Span
   b. Digit Symbol

5. Grooved Pegboard

6. Odd Man Out

7. Verbal Fluency – FAS

8. Animal Naming

9. Trailmaking Test
   a. Part A
   b. Part B

10. Clock Drawing
Appendix E: Sleep Study Flyer

New Sleep Study

● If you are currently in the memory study and you are:
  ○ 50 years old or older (HIV positive or negative) or
  ○ 20-40 years old and HIV positive

We would like to know more about how you are sleeping and how it might effect your memory testing

● Two different ways to participate:
  ○ Just answer some questions about your sleep - Only takes a few minutes!!
  ○ Wear a wrist actigraph to record sleep- Just like wearing a wrist watch!!

● If interested, let Kathrine or Jim know when you call to schedule your annual visit. (They will check other requirements to see if you are eligible
Appendix F: Letter Sent to older HIV Negative Participants

Important information regarding The Memory Study

Dear past Study Participant,

To help further our understanding of HIV and aging, you have been selected for an additional study visit for the HIV Seropositivity, Aging, and Cognitive Function study, “The Memory Study”, at the University of Hawaii. This visit will give us more information on long-term memory and thinking problems, and help us understand memory problems in older people with HIV.

If you are interested in participating in another visit, please call our office. You will be asked to sign an additional consent for the portion of the study. This visit will be the same as other study visits. You will receive compensation for your time for this visit to help pay for the costs of coming in for the visit such as transportation costs, as you have been in the past.

Thank you for helping us study memory and thinking problems within our community.

Sincerely,

Victor G. Valcour, MD
Associate Professor
Appendix G: Sleep Study Visit Protocol

For pts wearing the Actigraph

Forms and Protocol for first appointment: 3-7 days before annual visit:
- Consent
- Review instructions on wearing actigraph
- Review instructions for completing sleep diary
- Make arrangements for a reminder call if participant is taking the actigraph 1 to 2 days before the actigraph needs to be worn. Call Kathrine with information if a reminder call needs to be made.

Forms and Protocol for Annual visit:
- Collect actigraph and sleep diary
- Have participant fill out Pittsburgh Sleep Quality Index
- Have participant fill out Brief Fatigue Inventory
- Hand out Sleep pamphlet
- Pay participant ($10)

For pts doing Questionnaires only (no actigraph):

Forms and Protocol for Annual Visit:
- Consent
- Sleep Diary (for last night only)
- Pittsburgh Sleep Quality Index
- Brief Fatigue Inventory
- Sleep pamphlet
Appendix H: Informed Consent

Hawaii AIDS Clinical Research Program
University of Hawaii School of Medicine

I. Investigators
Victor Valcour MD, Kathrine Fast MA, Cecilia Shikuma MD, Dominic Chow MD, Michael Watters MD, Larry Day MD, Bruce Shiramizu MD.
3675 Kilauea Ave., Leahi Hospital, Sinclair Room 202, Honolulu, Hawaii 96816.
Phone: (808) 737-3012.

II. Title
Sleep disturbance in aging HIV positive individuals: A pilot study within the Hawaii Aging with HIV Cohort.

III. Informed Consent
You are being asked to take part in this research study because you are currently participating in the Neurocognitive Function: HIV Seropositivity and Aging study (the “Memory Study”), a study that is part of the Hawaii AIDS Clinical Research Program. The Memory Study is sponsored by the National Institutes of Health (NIH). This added study on sleep is sponsored by the NIH and the Hawaii Community Foundation (HCF). The doctor in charge of this study is Dr. Victor Valcour. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives information about this study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Before you learn about the study, it is important that you know the following:

- Taking part is of your own free will.
- You may decide not to take part in the study or stop being in the study at any time without it making any difference to your care now or in the future, or to any benefits you are allowed.

IV. Why Is This Study Being Done?
The purpose of this study is to look at how well people who are 50 or more years old and living with HIV sleep. We plan to compare how well these people sleep to people who are HIV negative. We also plan to compare them with people who are younger (20 to 40 year olds) and living with HIV. The study will also look at how memory and thinking may be affected by how well you sleep.

V. What Do I Have To Do If I Am In This Study?
In addition to your regular yearly visit for the memory and thinking study, you will be asked to wear a wrist actigraph for three days and answer questions about your recent sleep and level of fatigue (how tired you feel). A wrist actigraph looks like a wrist watch.
It will keep a record of your movement that will tell us how well you slept. You will visit the clinic 2 to 3 days before your annual visit for the memory study to get the wrist actigraph and begin wearing it.

We will also ask you to answer questions about your recent sleep and level of fatigue (how tired you feel) at the time of your annual visit for the memory study. These questions should take about 15 minutes to complete. If you do not wish to wear the wrist actigraph for 3 days, but are still interested in being part of the sleep study, you may take part in this study by answering the questions about sleep and fatigue at the time of your annual visit.

The procedures that are involved in this study are:

1. You will come to the clinic to pick up the wrist actigraph. It will be fitted on your wrist, just like a wristwatch. The visit will take approximately 15 to 30 minutes. This actigraph will be worn for 3 days, both during the day and at night. Each night as you go to bed, you will press a button on the actigraph. In the morning when you wake up, you press a button on the actigraph. Each morning you will fill out a short sleep diary which will take about 5 minutes to complete.

2. During your regular annual visit for the memory study, you will be asked some questions about your sleep for the past month and how rested you feel. These questions should take about 10 minutes to complete. You will return the actigraph to the research assistant at the time of your annual visit.

3. If you choose to participate in the sleep study, but do not want to wear the actigraph, you will be asked some questions about your sleep for the past month and how rested you feel at the time of your annual visit. The questions will take about 15 minutes to complete.

VI. How Many People Will Take Part In This Study?
About 150 people will take part in this study.

VII. How Long Will I Be In This Study?
The wrist actigraph part of this study will take about 3 days. If there are problems with use of the actigraph or scheduling of your appointments, this may take more time, but we expect it should usually be less than one week total. The sleep surveys take approximately 15 minutes at the time of your annual visit.

VIII. What Are The Risks Of The Study?
There is a slight risk that the actigraph may feel uncomfortable to wear, particularly if you are not used to wearing a watch.

IX. Are There Benefits To Taking Part In This Study?
There may be no direct benefits to you for taking part in this study. It may help you understand more about how well you sleep. If you agree, at the end of the study, we will send a brief summary of your sleep to your doctor. Things that are learned from this study may help us know how sleep might affect someone with HIV.
X. Compensation
If you participate in the wrist actigraphy part of the study, you will need to come into the office for a separate visit before your annual visit and we will provide $10 to cover your costs for that visit.

XI. What About Confidentiality?
All study information will be confidential (private) to the extent permitted by state and federal law and will not be given to anyone without your written consent (permission). A code, which will be known only to study personnel, will be used instead of your name on our study records. The code will be stored in a locked file cabinet.

We will do everything we can to protect your privacy. Also, no publication of this study will use your name or identify you personally.

People who may review your records include: University of Hawaii Committee on Human Studies (CHS), National Institutes of Health (NIH), Hawaii Community Foundation (HCF), study staff or study monitors. Our efforts to keep confidentiality does not stop you from releasing information about yourself and your taking part in the study. If the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will be required to tell the proper authorities.

XII. What Are The Costs To Me?
There are no direct costs to you to participate in this study.

XIII. What Happens If I Am Injured?
If you are injured (hurt) as a result of being in this study, a doctor or nurse at the Hawaii AIDS Clinical Research Program will give you immediate treatment for your injuries. You will then be told where you may get other treatment for your injuries. The cost for this treatment will be charged to your insurance company or to you. Your insurance company may not pay for these costs. If you are injured in the course of this research procedure, you alone may be responsible for the costs of treating your injuries.

The National Institutes of Health and the Hawaii AIDS Clinical Research Program has no money to pay you or compensate you in any way for injuries you may suffer. There is a research doctor on call 24 hours a day who can be reached through Physicians Exchange at 566-5036. You will not be giving up any of your legal rights by signing this consent form.

XIV. What Are My Rights As A Research Participant?
Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. You will be treated the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare or willingness to stay in the study.
XV. What Do I Do If I Have Questions or Problems?
If you have questions or problems with the actigraph during the time you are wearing it, please contact Kathrine Fast at (808) 737-3012 (regular working hours). After hours, you can reach the doctor on call by calling physician’s exchange at 566-5036.

If you have questions about this study or a research-related injury, you should contact Dr. Victor Valcour at (808) 737-3012 or the doctor on call through physician’s exchange at 566-5036 right away.

If you have questions about your rights as a research participant you may contact the Committee on Human Studies, University of Hawaii, 2540 Maile Way, Honolulu, Hawaii, 96822, phone: (808) 539-3955, email: uhirb@hawaii.edu

XVI. Voluntary Consent and Certification.
I take part in this study of my own free will and I can stop at anytime for any reason and this will not make a difference in the care I receive. My consent does not take away any of my legal rights in case of negligence or carelessness of anyone working on this project. I verify that I have read the above or that it has been read to me and that my permission is freely given. A copy of this consent has also been given to me.

XVII. Signatories
I agree to take part in this study.

1. ________________________________________________________________________
   Participant’s Name (Print)  Signature  Date

2. ________________________________________________________________________
   Name of Legal (Print)  Signature  Date
   Authorized Representative

3. ________________________________________________________________________
   Researcher’s Name (Print)  Signature  Date
   Researcher’s Representative

4. ________________________________________________________________________
   Name of Witness (Print)  Signature  Date
   to signature only
Appendix I: Actiwatch Instructions

Wrist Actigraph: instructions to the participant:

This is an actigraph. It is used to measure motor activity over several days. There are a few simple instructions to follow:

1) Wear the actigraph on your non-dominant wrist, just like a watch (if you write with your right hand, wear it on your left wrist) for the entire 3 days. Wear the actigraph on the same wrist for the complete test period.

2) The actigraph is water-proof. It can stay on your wrist for showers, or swimming in a pool. The only time you would need to take off the actigraph is to swim in the ocean.

Please DO NOT wear the actigraph when swimming in the ocean. If you are going to the beach to swim or surf- you can take off the actigraph and leave it at home. Put it back on when you return.

When you take the off the actigraph for any reason- record the date and times on the bottom of the sleep diary (e.g., 8/8/05; actigraph off from 3pm to 5pm).

3) Twice each day you will press the event marker (button) on the actigraph. You will hear a “click” that lets you know the marker has been activated.

Press the marker:
   1) Each night when you go to bed and turn off the lights,
   2) Each morning when you awake and get out of bed

If you remember that the marker should have been activated more than 5 minutes later than the instructed time, do not activate.

If you have any questions or problems with the wrist actigraph, please call Kathrine at 441-1585.
Appendix J: Sleep Study Pamphlet

Getting a Good Night’s Sleep:
There are several things you can do try to improve your sleep. This pamphlet outlines how you can help yourself.

If you continue to have trouble sleeping, consult your doctor to see if another treatment is right for you.

A doctor may:

- Treat or refer you to a professional for behavioral treatments that have been shown to work with insomnia, such as cognitive behavioral therapy, sleep restriction or stimulus control treatments or relaxation training.
- Review your medications to see if they may be causing the problem and alter medication if possible.
- Treat your insomnia with short term use of sleep medication. Since some medications can cause sleep disturbances when you stop using them, follow your doctors advice regarding how to use them and how to discontinue their use.
- Recommend short term use of over-the-counter sleep (OTC) aids. OTC medications should not be used for people with certain medical conditions or who use some types of medications or other substances. Your doctor can advise you on using them safely.
- Refer you to a professional for treatment of depression or anxiety.

What you can do:
Making simple changes in these areas may improve your sleep:

3 Your Personal Habits
- Avoid substances that can interfere with sleep for several hours before bed.
- Regular exercise.
- A regular sleep and wake schedule.

3 Your Sleeping Environment
- Keep your room cool, dark and as noise free.
- Reserve your bedroom for sleep only.

3 Getting Ready For Bed
- Do things that are quiet and relaxing during the hour or so before going to bed.
- Get up and do something else if you can’t get to sleep in 15-30 minutes.

Some Specific Tips for a Good Night’s Sleep

⇒ Establish and maintain a regular bedtime and arising time. Get up at the same time every day, even if you had trouble sleeping the night before.

⇒ Exercise regularly. Exercise in moderate amounts, early in the day.

⇒ Keep your bedroom at a comfortable temperature of 72° or less, if possible. A hot room can cause more awakenings, more body movements, and less deep sleep temperature. Choose a room or make your bedroom as dark and noiseless as possible.

⇒ Let your body know that the bed is associated with sleeping only; read and watch TV etc. in another room.

⇒ Allow yourself a “winding down” time prior to going to bed. Reading, taking a bath, meditation or relaxation techniques may help.

⇒ Determine your optimal amount of sleep. For example, some people need 9 hours of sleep to feel good, but others may only need 7 hours. Sleep only as much as you need; oversleeping can make you even more tired.
Don’t

⇒ Don’t drink beverages with caffeine (e.g., coffee, tea, soft drinks), or take substances with caffeine (e.g., chocolate, Excedrin®) after dinner.

⇒ Don’t eat late evening meals or drink large quantities of liquids in the evening. If hungry, eat a light snack. Avoid high protein or spicy foods.

⇒ Don’t use alcohol to help you fall asleep. Alcohol may help you relax so that you fall asleep, but your sleep will not be sound.

⇒ Try not to smoke in the evening. Tobacco acts as a stimulant that can disturb sleep.

⇒ Don’t exercise strenuously within 2 hours of bedtime. It may wake you up too much to fall asleep.

⇒ Don’t take long naps during the day or evening. If you need to rest, try a 15-20 minute midday nap. It can be refreshing without interfering with getting to sleep later.

⇒ Don’t watch TV, eat, or read in bed.

⇒ Don’t lie awake in bed for long periods of time. If you can’t fall asleep in 15-30 minutes, get out of bed and do something relaxing before trying to fall asleep again. The more stress you feel about trying to get to sleep, the harder it will be to fall asleep.

Below are some examples of books or websites available for more information about insomnia:

Books:

No More Sleepless Nights (1996)
Peter Hauri, Ph.D., & Shirley Linde, Ph.D.

No More Sleepless Nights Workbook (2001)
(A workbook to accompany “No More Sleepless Nights)
Peter Hauri, Ph.D., Murray Jarman, & Shirley Linde, Ph.D.

Get a Good Night’s Sleep (1996)
Katherine A. Albert, M.D., Ph.D.,

Websites:

National Sleep Foundation – brochures
www.sleepfoundation.org/
(click on “publications”)

Everything you wanted to know about sleep but were too tired to ask
www.sleepnet.com

Sleep Medicine Home – links to sleep information
www.users.cloud9.net/~thorpy/

References:

- www.sleepfoundation.org

Some Important Facts About Sleep

Everyone has trouble sleeping from time to time. If you have difficulty falling asleep or staying asleep, you may have insomnia. Insomnia can last for a few days (transient), weeks (short-term) or months (chronic).

According to the National Sleep Foundation, insomnia is a symptom, not a disorder in itself. Insomnia can be a symptom of several different types of problems:

- Medical/physical problems (e.g., sleep apnea, medical conditions that cause pain, other medical conditions)
- Stress or depression
- Side effect of medications (blood pressure or heart disease medications, anti-retroviral medications, pain medications are examples of medications that may cause disruption to sleep.

Below are some examples of books or websites available for more information about insomnia:

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- Medical/physical problems (e.g., sleep apnea, medical conditions that cause pain, other medical conditions)
- Stress or depression
- Side effect of medications (blood pressure or heart disease medications, anti-retroviral medications, pain medications are examples of medications that may cause disruption to sleep.
Appendix K: Form Letter to Primary Care Physician

Date
XX, MD

Dr.XX, re: Pt name, DOB

(Pt name) was examined on (date) as a participant in the **Neuro-cognitive Function Study** at the University of Hawaii. In addition to data normally collected for this study, the participant also agreed to wear a wrist actigraph. The wrist actigraph measures movement and is used in research to estimate sleep indices. The actigraph was worn for three days and nights, ending on the morning of the study visit.

We do not provide diagnoses, medical advice, nor treatment and all participants are referred back to their own physicians for regular medical care.

**Actigraph Data:**

Results reported are an average of the 2\textsuperscript{nd} and 3\textsuperscript{rd} night recordings for the 3 night study.

Total hours slept: XX

Sleep efficiency: XX % (time asleep compared to time in bed)

Sleep latency: XX minutes (estimated time taken to initially fall asleep).

Thank you again for allowing your patients to participate in this valuable project. I hope the information above is useful. Please feel free to contact me if you have further questions.

Sincerely,

Victor G. Valcour, MD, FACP
Assistant Professor
Appendix L: Glossary of Medical Terms

Acquired Immune Deficiency Syndrome (AIDS): AIDS is a disease of the human immune system caused by the human immunodeficiency virus (HIV). This condition progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumors. A T-helper lymphocyte count of below 200/mm³, or one of several opportunistic infections or malignancies (criteria developed by the Centers for Disease Control), along with the presence of the HIV virus, constitutes a diagnosis of AIDS.

Cluster of differentiation 4 (CD4+): A membrane protein or receptor of T-helper lymphocytes. It is the attachment site for the HIV virus.

Highly active anti-retroviral therapy (HAART): A form of anti-HIV treatment that usually includes a combination of protease and reverse transcriptase inhibitors whose purpose is to reduce the HIV viral load to undetectable levels.

Human Immunodeficiency Virus (HIV): A retrovirus of the lentivirus class, formerly called LAV or HTLV-III that can cause AIDS. A lentivirus is a virus that produces disease with a greatly delayed onset and protracted course such as HIV.

The Multi-Center AIDS Cohort Study (MACS): The Multicenter AIDS Cohort Study (MACS) is an ongoing prospective study of the natural and treated histories of HIV-1 infection in homosexual and bisexual men conducted by sites located in Baltimore, Chicago, Pittsburgh and Los Angeles. A total of 6,972 men have been enrolled. From April 1984 through March 1985, 4954 men were enrolled; an additional 668 men were enrolled from April 1987 through September 1991. A third enrollment of 1350 men took place between October 2001 and August 2003. This third cohort augments research efforts in the long-term benefits and adverse effects of therapy.

Mini Mental Status Exam (MMSE): The mini-mental state examination (MMSE) is a brief 30-item examination used as a screen for cognitive impairment. It is typically used in medical settings to screen for dementia.

Memorial Sloan Kettering Dementia Scale (MSK) scale: The MSK scale utilizes data from neurological, neuropsychological, and quality of life (ability to engage in activities of daily living) measures.

Multivariate Odds Ratio (MOR): An estimate of Risk Ratio (see definition below) in a case-controlled study (i.e., participants are selected based on disease status), where it would not be possible to calculate the natural rate of development of a given disease or condition. The Odds Ratio is a calculation of the ratio of the odds of exposure to a given risk factor among the study cases to that among the control group.

Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI): A member of a class of anti-retroviral medications that works to directly combine with and block the action of HIV’s
reverse transcriptase (a viral enzyme that transcribes viral RNA into DNA so that genetic material of the virus can be integrated into genetic material of the T-Helper cell).

*Risk Ratio or Relative Risk* (RR): Estimates the magnitude of an association between exposure (or identified risk factor) and disease, and indicates the likelihood of developing the disease in the exposed group relative to those who are not exposed. It is defined as the ratio of the incidence of disease in the exposed group, divided by the incidence of disease in the non-exposed group.

*Viral Load*: The amount of HIV RNA per unit of blood plasma. Viral load is utilized as an indicator of HIV virus concentration and reproduction rate. The number is expressed as numbers of copies of HIV RNA genome per milliliter of plasma.
Appendix A: Summary Table of Epidemiologic Sleep Studies in Human Immunodeficiency Virus (HIV) Research

<table>
<thead>
<tr>
<th>Reference</th>
<th>Participants</th>
<th>Gender</th>
<th>Sleep Measures</th>
<th>Study Goals</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Cruess et al., 2003)</td>
<td>57 HIV pos</td>
<td>41/16</td>
<td>Pittsburg Sleep Quality Index (PSQI)</td>
<td>Correlations between sleep disturbances, T-cell counts and distress as measured by the Impact of Events Scale (IES)</td>
<td>1) Mean PSQI score = 6.7 (SD= 3.8). Sixty-one % had a PSQI score of &gt; 5. 2) Sleep mediates the relationship between T-cell counts and distress ($\Delta R^2 = .12$, $\Delta F(5,51) = 4.31$, $P&lt;.01$)</td>
</tr>
<tr>
<td>(Darko, McCutchan, Kripke, Gillin, &amp; Golshan, 1992)</td>
<td>62 HIV pos/ 50 HIV neg</td>
<td>62/0 50/0</td>
<td>Questionnaire developed for study</td>
<td>Compared sleep, fatigue and disability indices of HIV neg, HIV pos men with AIDS*, and HIV pos men without AIDS</td>
<td>HIV pos participants were significantly more likely to sleep more, nap more, and feel fatigued more often.</td>
</tr>
<tr>
<td>(Hodges &amp; Buboltz, 2004)</td>
<td>125 HIV pos</td>
<td>85/37/3</td>
<td>Sleep Quality Index, Sleep Habits</td>
<td>Description of sleep habits</td>
<td>1) 40% of sample reported “poor sleep quality”</td>
</tr>
</tbody>
</table>
Sleep and psychomotor slowing in older HIV

Questionnaire

1) Mean PSQI = 9.0 (SD = 4.4)
2) Mean GSDS = 64.6 (SD = 21.4)
3) Actigraph means: Total sleep time – 6.5 hours (SD = 2)
Sleep efficiency = 74.7% (SD = 19)

Correlations between sleep patterns and self-reported fatigue levels

1) Correlates of sleep quality: CES-D, Spielberger State and Trait Anxiety, HIV Assessment Tool-symptom and general well-being scale, Epworth Daytime Sleepiness scale
2) Health Status variables (symptom severity, general well-being, depressive symptoms, daytime sleepiness, state anxiety) explained 43% of the variance in sleep quality ($F = 7.93, p < 0.000, df = 52$)

(100 HIV pos 0/100 Actigraph, General Sleep Disturbance Scale (GSDS), Pittsburgh Sleep Quality Index)

(Nokes & Kendrew, 2001)

(58 HIV pos Not given Pittsburg Sleep Quality Index)

(Norman et al., 14 HIV pos / 14/0 Polysomnography,)

Describe sleep patterns
1) PSQI mean for HIV pos = 3.5,
Sleep and psychomotor slowing in older HIV

1992) 10 HIV neg 10/0 Pittsburg Sleep Quality Index SD = 1.9

2) HIV pos polysomnography = wakefulness, Stage 3 & 4, and REM sleep more evenly distributed throughout night.

(Robbins, Phillips, Dudgeon, & Hand, 2004) 79 HIV pos 36/43 Pittsburg Sleep Quality Index, Epsworth Daytime Sleepiness Scale

Sleep quality predicted by pain, depression, state anxiety, HIV-related symptoms and demographic factors.

1) Mean PSQI score = 12.3 (SD = 3.9)

2) Fatigue and total pain explained 34% of variance in sleep quality.

(Rubinstein & Selwyn, 1998) 115 HIV pos 79/36 Pittsburg Sleep Quality Index

Describe sleep patterns

1) 73% of participants had a PSQI score of >5 (>5 = sleep disturbance)

(Wheatley & Smith, 1994) 45 HIV pos (42/3) Wheatley Stress Profile-sleep section

Describe sleep patterns

Compared to controls, HIV pos participants had sig worse sleep onset times, nocturnal awakenings, and well-being upon awakening.

(White et al., 1995) 23 HIV pos/13 HIV neg (23/0) Polysomnography; Fatigue and sleep

Compared HIV pos and HIV neg sleep indices

1) no significant differences in total sleep time, sleep latency, subjective
Sleep and psychomotor slowing in older HIV

questionnaire

sleep quality.

2) HIV+ participants with >400 x 10⁶/ℓ CD4b counts had a greater % Slow wave sleep in 2nd and 3rd parts of the night (t = 1.82; df, 22; P<0.04) and (t = 1.95; df, 22; P<0.03) compared to HIV+ with < 400 x 10⁶/ℓ CD4 counts

(Vance & Burrage, 2005) 50 HIV pos/ 50 HIV neg Not given Author generated sleep questions

Compared HIV post and HIV neg sleep indices, compared sleep indices of younger and older HIV pos

1) No sig differences in #hours slept between HIV pos (Mean = 6.73 SD = 2.15) and neg (Mean = 6.77, SD = 1.25).

2) Age was not sig related to sleep indices.

Note: a = Acquired Immune Deficiency Syndrome; b = A membrane protein or receptor of T-helper lymphocytes; is the attachment site for HIV (Kalichman, 1998)