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Sleep, Fatigue, and Problems with Cognitive Function in Adults Living with HIV

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Abstract

Up to 50% of people living with HIV have some neurocognitive impairment. We examined associations of sleep and fatigue with self-reported cognitive problems in 268 adults living with HIV. Multivariate regression was used to examine associations between cognitive problems, self-reported sleep quality, actigraphy-measured total sleep time and wake after sleep onset, and fatigue severity. Poorer self-reported sleep quality ($p < .001$), short or long total sleep time (< 7 or > 8 vs. 7–8 hours, $p = .015$), and greater fatigue ($p < .001$) were associated with lower self-reported cognitive function scores after controlling for demographic and clinical characteristics. However, objective measure of wake after sleep onset was unrelated to self-reported cognitive function scores. Findings suggest that assessing and treating poor sleep and complaints about fatigue would be areas for intervention that could have a greater impact on improving cognition function than interventions that only target cognitive problems.

Keywords

cognition; fatigue; HIV; sleep

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Disclosures

The authors report no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

Up to 50% of people living with HIV (PLWH) have some neurocognitive impairment (Heaton et al., 2010; McArthur, Steiner, Sacktor, & Nath, 2010), especially in the domains of concentration, attention, and working memory (Ances & Ellis, 2007). Worldwide, approximately 4.2 million PLWH were older than 50 years of age in 2013 (Mahy, Autenrieth, Stanecki, & Wynd, 2014). As the population of PLWH ages, the normal process of aging may contribute to cognitive impairment in this patient population. Age-related comorbidity (Valcour, 2013), inflammatory processes, and cytokine activity (Kraft-Terry, Stothert, Buch, & Gendelman, 2010) also influence cognitive impairment in HIV infection. Schouten, Cinque, Gisslen, Reiss, and Portegies (2011) reported in their review article that risk factors for developing an HIV-associated neurocognitive disorder included CD4+ T cell nadir, aging, microbial translocation, anemia, thrombocytopenia, host genetic factors, and viral genetic factors.

Sleep disturbance and fatigue are prevalent symptoms in HIV disease; up to 75% of PLWH experience sleep disturbance (Rubinstein & Selwyn, 1998) and up to 88% experience fatigue (Jong et al., 2010; Millikin, Rourke, Halman, & Power, 2003). We also previously reported high rates of difficulty sleeping (56%) and lack of energy (65%) in our current sample of adults living with HIV (Lee et al., 2009). Sleep disturbance has been related to cognitive impairment in other populations such as older adults or individuals with heart failure (Blackwell et al., 2014; Garcia et al., 2012). Fatigue in HIV has also been well studied (Jong et al., 2010) and is often associated with sleep disturbance (Millikin et al., 2003). However, little is known about the effects of sleep disturbance and fatigue on how cognitive problems are perceived by the patient with HIV, and underlying mechanisms are still not clear.

Mild neurocognitive disorder and asymptomatic neurocognitive impairment are more prevalent than HIV-associated dementia (Valcour, 2013). Cognitive impairment in HIV can affect adherence to antiretroviral therapy (ART) or lead to difficulty managing complex medical regimens related to comorbidities (Schouten et al., 2011). It is, therefore, important to identify factors related to problems with cognitive function. If sleep disturbance and fatigue are associated with poor cognitive function in HIV disease, strategies that improve poor sleep and address complaints about fatigue could also improve cognitive function and quality of life in this population. Thus, the purpose of our study was to examine associations of sleep and fatigue with self-reported cognitive problems in adults living with HIV.

Methods

The Symptom and Genetic Study is a longitudinal study with a convenience sample of adults living with HIV aimed at identifying biomarkers of symptom experiences in HIV-infected adults (Lee et al., 2009). A cross-sectional analysis was conducted to examine the relationships between perceptions of cognitive function, subjective and objective measures of sleep, and fatigue, while controlling for demographic and clinical characteristics. The Committee on Human Research at the University of California, San Francisco, approved the study. Study participants were recruited using flyers at HIV clinics and community sites in the San Francisco Bay Area. All participants provided written informed consent and signed a Health Insurance Portability and Accountability Act release to access their protected medical information.

Participants were included if they were English-speaking adults, at least 18 years of age, and had been diagnosed with HIV at least 30 days before enrollment. To specifically address HIV-related symptom experiences, potential participants were excluded if they were currently using illicit drugs (as determined by self-report or by positive urine drug testing); worked nights (at least 4 hours between 12 am and 6 am); reported having bipolar disorder, schizophrenia, or dementia; or had been pregnant within the prior 3 months. Participants with insomnia were not excluded, but those with other diagnosed sleep disorders, such as apnea and narcolepsy were excluded.

Sample Characteristics

Demographic characteristics of age, gender, race/ethnicity, education, disability, and income were collected using a demographic questionnaire. Prior AIDS diagnosis and current medication regimen were obtained through self-report. The most recent CD4+ T-cell count, HIV viral load values, and hemoglobin values to determine anemia were obtained from patient medical records. Medications were categorized as ART, sleep, antidepressant at therapeutics dose, or opiate, based on the potential for such medications to impact cognition. Trained research staff obtained measures of body mass index (BMI, weight in kilograms divided by squared height in meters) during a Clinical Research Center clinic appointment.

Subjective Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI) was used to measure subjective sleep quality and types of sleep disturbances over the previous month (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The scale included 19 items and 7 component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The component scores have usually been scored on a scale of 0 to 3, but the raw scores for each component were used in our analysis to better capture variation in the measured construct. The global sleep quality score was a summation of the seven component scores and could range from 0 to 21, with higher scores indicating poorer sleep quality. A global PSQI score of greater than 5 was a sensitive and specific measure of poor sleep quality. The scale has demonstrated good reliability and validity across many patient populations (Buysse et al., 1989).

Actigraphy Sleep Duration and Disruption

Sleep was objectively estimated with a noninvasive battery-operated wrist actigraph microprocessor with a piezoelectric beam that detected movement and acceleration (Mini Motionlogger Actigraph, AAM-32 Ambulatory Monitoring, Inc. Ardsley, NY). Actigraphy provided continuous movement counts and data were sampled in 30-second epochs using zero-crossing mode. Participants wore the actigraphy monitor continuously on the non-dominant wrist for 72 hours on three consecutive weekdays between Monday and Friday to control for potential weekend variability and to reduce subject burden in this chronically ill patient population. Participants also completed sleep diaries each morning and evening of the actigraphy monitoring period to cross-validate bed times and wake times. Wrist actigraphy has been validated with polysomnography measures of sleep and wake time for healthy and disturbed sleepers (Lichstein et al., 2006). Bed time and final wake times were determined by one of two approaches: (a) participant pressing the event marker on the

actigraph to indicate *lights out* and *lights on* or (b) if no reliable event marker indication existed, the diary entry of clock time was used if it matched with a 50% change in movement during the same 10-minute block of time on actigraphy.

Actigraphy-based total sleep time (TST) and wake after sleep onset (WASO) were determined using the Cole–Kripke algorithm from the automatic sleep-scoring program (Action4® Software Program, Ambulatory Monitoring Inc., Ardsley, NY) to reduce researcher scoring bias. WASO was standardized as a percentage of the person's TST to control for varying sleep durations. The intraclass correlation coefficient across the 3 nights was 0.83 for WASO and 0.76 for TST. The 3-night means for TST and WASO were then used for analyses.

Fatigue Severity

A 4-item version of the Lee Fatigue Scale (LFS) was used to assess fatigue severity in the morning and evening (Lee, Hicks, & Nino-Murcia, 1991). This measure focused primarily on general fatigue and how participants were feeling right now rather than specific dimensions of fatigue (e.g., mental or physical) over a broader timeframe. Participants completed the LFS within 30 minutes prior to going to sleep to measure fatigue on 3 consecutive evenings and within 30 minutes of waking on 3 consecutive mornings. Evening and morning fatigue scores were calculated as the mean of the 4 items across the 3 days and could range from 0 to 10, with higher scores indicating greater fatigue. The LFS has been used to measure fatigue in healthy individuals, as well as in patients with HIV, and has established validity and internal consistency (Lee, Gay, Lerdal, Pullinger, & Aouizerat, 2014; Lee et al., 1991).

Perceived Problems with Cognitive Function

Self-reported problems with cognitive function were assessed with the Medical Outcome Study (MOS) Cognitive Functioning Scale (Stewart, Ware, Sherbourne, & Wells, 1992). The scale contains six items that assess the frequency during the previous month that one had experienced problems in six cognitive domains: reasoning, concentration and thinking, confusion, memory, attention, and psychomotor. Each item is rated from 1 (*all of the time*) to 6 (*none of the time*). The six items are summed to yield a score from 6 to 36, and the score is then converted to a 0–100 point scale, with higher scores indicating better perceived cognitive function. The MOS Cognitive Functioning Scale has been shown to be valid and reliable in previous studies of HIV-infected adults (Revicki, Chan, & Gevirtz, 1998).

Statistical Analysis

All analyses were performed using SPSS version 22 software for Windows (IBM Corporation, Armonk, NY). Data analysis included descriptive statistics to summarize demographic and clinical characteristics. CD4+ T cell count and HIV viral load were analyzed in clinically meaningful categories. Associations of demographic, clinical, sleep, and fatigue with cognitive problems were evaluated using Pearson correlations, independent sample *t*-tests, or analyses of variance with post hoc tests. Pearson correlations were also used to explore relationships between self-reported sleep quality, severity of fatigue, and problems with cognitive function.

Multivariate regression was used to examine associations between MOS cognitive function scores (0–100), subjective and objective measures of sleep, and morning and evening fatigue, with adjustments for covariates. Demographic variables were entered into the model first (Step 1), followed by clinical characteristics (Step 2), objective sleep measures (TST and WASO, Step 3), subjective sleep quality (Step 4), and morning and evening fatigue (Step 5). Age, gender, and education were forced into the model as covariates that would potentially impact cognitive problems, regardless of their associations with cognitive problems in Step 1. Other variables significantly associated with cognitive problems from the analysis in each step were retained in the final multivariate regression model. For all analyses, a p value < .05 was considered statistically significant.

Results

Sample Characteristics

A convenience sample of 350 adults with HIV was enrolled in the study; 33 participants were excluded prior to analysis for either screening positive for illicit drugs (n = 31) or being unable to submit a urine or blood sample (n = 2). An additional 28 participants were excluded due to incomplete or invalid actigraphy and 21 were excluded due to missing data for PSQI, fatigue, cognitive function, CD4+ T cell, or viral load. Eleven participants were missing valid actigraphy data for the initial visit; all data from a subsequent visit were used instead. The remaining 268 adults were included in this analysis. Table 1 summarizes the demographic and clinical characteristics of the final sample. The mean age was 45 ± 8.5 (*SD*) years, most (67%) were male, and fewer than half (42%) of the participants were White.

The mean PSQI score was 7.3 ± 3.6 (*SD*) and 63% had poor sleep quality using a cutoff point of 5 (Table 2). The mean TST was 6.2 hours ± 1.6 (*SD*), and 18% of participants slept between 7 and 8 hours. The mean WASO was 20.5% ± 14.7 (*SD*). The mean score for morning fatigue was 3.4 ± 2.3 (*SD*) and evening fatigue was 5.1 ±2.7 (*SD*). The mean MOS Cognitive Functioning Scale score was 71.0 ± 24.0 (*SD*), and the full range of scores was 0 to 100 in this sample.

The only demographic variable associated with cognitive problems in the bivariate analysis was gender (p = .026), with transgender women reporting significantly lower cognitive function than males (Table 1). Sleep medication use was the only clinical variable associated with cognitive problems (p = .013). CD4+ T cell count (< 200 vs. ≥ 200 cells/mm^3), HIV viral load (detectable vs. undetectable), age, race, antidepressant use at therapeutic dose, anemia, and body mass index (BMI) were not significantly associated with MOS cognition scores in the bivariate analysis, nor were other demographic, clinical, or laboratory characteristics.

In the bivariate analysis, participants with PSQI greater than 5 reported more cognitive problems than those with PSQI of 5 or less (p < .001; Table 2). Short or long TST (< 7 or > 8 hours), when compared to TST between 7 and 8 hours, was also associated with more cognitive problems (p = .007). A correlation matrix of WASO, TST, sleep quality, morning fatigue, evening fatigue, and cognitive problems is included in Table 3. Self-reported

cognitive problems were correlated with poorer sleep quality ($r = -.378$, $p < .001$) and greater morning fatigue ($r = -.356$, $p < .001$) and evening fatigue ($r = -.210$, $p = .001$), but there was no relationship between problems with cognitive function and objectively measured TST ($r = .033$) or WASO ($r = .007$).

Multivariate regression analysis revealed that 25% of the variance in self-reported cognitive problems ($p < .001$) was explained by sleep quality, TST, morning fatigue, and covariates including age, gender, education, and sleep medication use (Table 4). Poorer subjective sleep quality ($p <. 001$), shorter or longer TST (< 7 or > 8 hours vs. 7–8 hours, $p = .015$), and greater morning fatigue ($p < .001$) were associated with cognitive problems, even after controlling for demographic and clinical variables. Gender was a significant demographic variable associated with self-reported cognitive problems in the multivariate analysis, with transgender women reporting more cognitive problems than men ($p = .027$). Sleep medication use was significantly associated with cognitive problems in Step 2 ($p = .011$), but the significance of the association disappeared in the final model shown in Table 4. When adding morning and evening fatigue in Step 5, evening fatigue was not associated with cognitive problems and thus evening fatigue was not retained in the final model.

Discussion

The major finding from our study was that self-reported sleep quality, TST using wrist actigraphy, and fatigue were significantly associated with perception of cognitive problems in adults with HIV, even after controlling for relevant demographic and clinical variables. However, disrupted nighttime sleep (WASO) was unrelated to perception of cognitive problems.

Cognitive impairment is a critical emerging issue in HIV infection because PLWH are living longer due to improvements in ART (Valcour, 2013). HIV-infected adults have symptomatic and asymptomatic HIV-associated neurocognitive disorders that reflect a spectrum of neurocognitive impairment, even in optimally treated patients with HIV (Gamaldo et al., 2013; Valcour, 2013). Studies have shown a variety of host and viral factors related to developing HIV-associated neurocognitive disorders (Jayadev & Garden, 2009).

Our study revealed that participants who reported more problems with cognitive function also had poorer self-reported sleep quality, sleep duration that was shorter or longer than 7 to 8 hours, and more severe fatigue, but the objective measure of sleep disruption (i.e., WASO) was unrelated to cognitive function. Both morning and evening fatigue were independently associated with self-reported problems with cognitive function; evening fatigue was not significant in the multivariate analysis, while morning fatigue remained significantly associated with cognitive function. In healthy adults, sleep deprivation has been associated with higher levels of morning fatigue (Morris, So, Lee, Lash, & Becker, 1992), which suggests that morning fatigue may be related more to the prior night of sleep disturbance, while evening fatigue may be more related to activities that occurred during the day.

Despite the absence of an association between cognitive problems and WASO in our study, shorter and longer sleep duration (TST < 7 or > 8 hours vs. 7–8 hours) was associated with cognitive problems. The results of studies on associations between sleep duration and cognitive function vary (Blackwell et al., 2014; Faubel et al., 2009; Xu et al., 2011). Studies in a general population have suggested a potential relationship between sleep loss and cognitive function. Sleep loss during the night may impair metabolism in the prefrontal cortex, the area of the brain that regulates aspects of cognition such as attention, alertness, and decision-making (Durmer & Dinges, 2005; Walker, 2009). It is possible that participants in our study had some impaired metabolism in the prefrontal cortex due to short sleep duration and poor sleep quality, which may have lead to poor cognition. Miyata et al.(2010) reported that sleep loss in healthy adults decreased cerebral blood flow in the frontal lobes and impaired daytime cognitive function. Impaired metabolism as well as decreased cerebral perfusion in the brain due to sleep loss may also be related to impaired cognition.

Long sleep duration has also been reported to significantly influence cognitive function, especially in older adults (Faubel et al., 2009; Xu et al., 2011). Our study revealed an association of longer and shorter sleep duration with cognitive problems in adults with HIV. The mechanisms underlying the relationship of longer sleep duration and cognition are still not well understood. The physiological demand for sleep and compensation for poor sleep quality may contribute to longer sleep duration (Faubel et al., 2009) and lead to impaired cognition.

Gamaldo et al. (2013) reported a relationship between cognitive function and sleep. They noted better cognitive performance on tasks of attention, frontal/executive function, and psychomotor/motor speed associated with polysomnography-recorded sleep parameters that included reduced WASO, longer sleep latency, and greater TST in PLWH on combination ART. However, self-reported sleep quality, daytime sleepiness, and actigraphy indices were not associated with cognition. Their sample size was relatively small (n = 33), and statistical power may have been a reason for the lack of statistical significance. While their sample was comparable in demographics (mean age = 49 years, 75% male), they reported a higher mean PSQI score (8.76 ± 4.03).

Gamaldo et al. (2013) also found little relationship between the 1 night of polysomnography sleep measures in the laboratory and the subsequent 2-week actigraphy measures in the home environment. In our sample, self-reported sleep quality and TST using wrist actigraphy were associated with self-reported problems with cognitive function, whereas self-reported sleep onset latency and WASO using wrist actigraphy were not associated with self-reported problems with cognitive function. One possible reason for these differences may be our use of the MOS Cognitive Functioning Scale as a global measure of perceived cognitive problems, whereas Gamaldo et al. (2013) included a battery of neuropsychological tests 2 weeks after polysomnography. It is unclear why cognitive problems were associated with TST and self-reported overall sleep quality as well as each component score in the PSQI, but were not associated with WASO measures in our study. A wrist actigraph recording approximated sleep as a behavioral measure, and WASO can be overestimated in restless sleepers and underestimated in sedentary adults. It is possible that perception of cognitive problems may influence an individual’s perceptions of sleep quality and fatigue

(Faubel et al., 2009; Xu et al., 2011). Self-reported sleep quality and fatigue remained significantly associated with cognitive problems, even after controlling for objective measures of sleep, sleep medication use, and other demographic and clinical characteristics. These associations underscored the importance of self-report measures of sleep and fatigue.

Between 33% and 88% of adults with HIV experience fatigue (Jong et al., 2010; Millikin et al., 2003). Our group has reported that the prevalence of lack of energy was 65% in this sample, but lack of energy was conceptually different from the report of feeling fatigued (Aouizerat, Gay, Lerdal, Portillo, & Lee, 2013). Researchers have related fatigue in HIV to depression, anxiety, sleep problems, comorbidity, and use of combined ART (Aouizerat et al., 2013; Jong et al., 2010). However, the relationship between fatigue and cognition in HIV is not well documented. Millikin et al. (2003) reported no association between neuropsychological testing and fatigue measured by the Fatigue Severity Scale, which assesses impact of fatigue on function. However, neurocognitive complaints were associated with fatigue. Our results of an association between fatigue and self-reported cognitive problems are consistent with these latter findings (Millikin et al., 2003). Taken together, these findings suggest that HIV-infected adults who complain about morning or evening fatigue should be further assessed for poor cognition.

One plausible mechanism relating sleep disturbance and fatigue to cognition may be common underlying biological mechanisms involving immune suppression and inflammation. After early HIV infection, HIV enters the brain and settles in perivascular macrophages and microglial cells (Gamaldo et al., 2013; Schouten et al., 2011). Replication of HIV in these cells triggers an immune response, produces viral and inflammatory proteins, and leads to neurological impairment (Schouten et al., 2011). In our sample, participants with detectable viral loads did not differ from participants with undetectable viral loads in self-report of cognitive problems. Other researchers have found that the patient's historically lowest CD4+ T cell count (nadir) was related to current cognition (Valcour et al., 2006; Valcour, 2013). In our study, participants with CD4+ T cell count lesser than 200 cells/mm^3 did not differ in self-reports of cognitive problems from participants with CD4+ T cell counts greater than 200 cells/mm^3.

Chemoattractant protein-1 (CCL2), tumor necrosis-factor alpha (TNF-α), interleukin (IL) 1 beta, IL-6, interferon gamma, and IL-15 have all been associated with neuronal injury in the brain and cognition in HIV (Kraft-Terry et al., 2010). We have reported that cytokine polymorphisms of IL1R2, IL2, and TNF-α predicted sleep maintenance as assessed by actigraphy-measured WASO in this sample of individuals with HIV infection (Lee, Gay, Pullinger, et al., 2014). We also revealed associations between cytokine polymorphisms of IL1B, IL4, and TNF-α and fatigue in this sample of HIV infected adults (Lee, Gay, Lerdal, et al., 2014). Although plasma cytokines and polymorphisms associated with sleep, fatigue, and cognition have varied in other studies, findings suggest these symptoms are associated with inflammatory mechanisms. Anti-inflammatory medication reduces sleepiness and fatigue in patients with sleep apnea (Vgontzas et al., 2004). Thus, assessing and treating the HIV inflammatory response may improve sleep and fatigue and potentially improve cognitive function in adults with HIV. Further research with longitudinal follow-up is

required to reveal possible inflammatory mechanisms underlying the relationship between sleep, fatigue, and cognition in HIV disease.

Sleep disturbance, fatigue, and impaired cognition are prevalent symptoms in adults with HIV. These symptoms may occur separately or co-occur. In our sample, poorer self-reported sleep quality, greater fatigue, and poorer cognitive problems were closely related. Our results suggest that these symptoms may occur as a symptom cluster. Symptom clusters can be defined as two or more concurrent symptoms that are related and may or may not have a common cause (Dodd, Miaskowski, & Paul, 2001). In samples of adults with HIV, symptom clusters have been reported for fatigue and depression (Voss, Portillo, Holzemer, & Dodd, 2007) and for fatigue and nausea (Cook, Sousa, Matthews, Meek, & Kwong, 2011). In samples of adults with cancer, symptom clusters for pain, fatigue, sleep disturbance, and depression (Illi et al., 2012) and pain, fatigue and sleep insufficiency (Dodd et al., 2001) have also been reported. However, concurrent symptoms of sleep disturbance, fatigue, and problems with cognition, or the cluster of these symptoms, in HIV have not been well studied and may provide clues to more tailored intervention strategies. Further study is required in patients living with chronic illnesses such as HIV and cancer in order to validate a potential symptom cluster that consists of poor sleep, fatigue, and problems with cognitive function.

Strengths of our study include the use of both self-report and objective measures of sleep and a relatively large sample that was demographically representative of the local population of PLWH. Limitations of our study include the cross-sectional design and use of a self-report measure of perceived problems with cognitive function. The decision-making capacity to consent to participate was one of the inclusion criteria in our study. Thus, more cognitively impaired adults with HIV were excluded, and these excluded adults may have experienced even more sleep disturbances and fatigue than what we describe in our sample. The MOS Cognitive Functioning Scale includes six cognitive domains (reasoning, concentration and thinking, confusion, memory, attention, and psychomotor) that people can have difficulty with on a daily basis, but further research using a battery of standardized neuropsychological assessments is warranted.

In summary, adults with HIV who experience poorer sleep quality, short or long sleep duration, or greater fatigue are more likely to report problems with cognitive function even after controlling for relevant demographic and clinical variables. Sleep disturbance, fatigue, and impaired cognition are major limitations to functional status and quality of life. Our findings suggest potential areas for intervention, as the assessment and treatment of poor sleep and fatigue may have more of an impact on patient experiences with cognitive function than treatment that focuses specifically on cognitive function.

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Key Considerations

- With successful treatments for HIV infection, PLWH are living longer, and cognitive impairment can become a significant problem in their daily lives.
- Poorer sleep quality, short or long sleep duration, and greater fatigue are associated with reports of poor cognitive function.
- It is important for clinicians to recognize and treat symptoms associated with poor sleep and fatigue, as this approach to treatment may have a greater impact on the patient's experiences with cognitive function.

Table 1

Self-reported Cognitive Problems by Demographic and Clinical Characteristics (n = 268)

	Mean ± *SD* or *n* (%)	Cognitive Problems Mean ± *SD*	Statistics
Demographic Characteristics			
Age, years (range = 22–77)	44.8 ± 8.5		$r = 0.059$, $p = .334$
< 50	187 (70%)	70.7 ± 24.4	$t_{(266)} = 0.29$, $p = .775$
≥ 50	81 (30%)	71.7 ± 23.0	
Gender			
Male	179 (67%)	73.5 ± 21.7	**$F_{(2,265)} = 3.69$, $p = .026$**
Female	67 (25%)	67.6 ± 26.4	
Transgender	22 (8%)	60.9 ± 30.7	
Race			
Caucasian	113 (42%)	73.1 ± 19.8	$F_{(2,265)} = 1.24$, $p = .291$
African American	100 (37%)	71.0 ± 26.4	
Other	55 (21%)	66.8 ± 26.8	
Education			
≤ high school	118 (44%)	70.2 ± 23.0	$t_{(266)} = 0.52$, $p = .605$
> high school	150 (56%)	71.7 ± 23.0	
Disability			
No	68 (25%)	75.3 ± 21.8	$t_{(266)} = 1.73$, $p = .085$
Yes	200 (75%)	69.6 ± 24.5	
Monthly Income			
< $1,000	186 (69%)	70.8 ± 24.2	$t_{(266)} = 0.24$, $p = .814$
≥ $1,000	82 (31%)	71.5 ± 23.5	
Clinical Characteristics			
CD4+ T-cell count			
< 200 cells/mm^3	46 (17%)	72.5 ± 25.8	$t_{(266)} = 0.45$, $p = .655$
≥ 200 cells/mm^3	222 (83%)	70.7 ± 23.6	
Viral Load (copies/mL)			
Undetectable	135 (50%)	73.5 ± 21.3	$t_{(253)} = 1.70$, $p = .091$
Detectable	133 (50%)	68.5 ± 26.3	
Ever Diagnosed with AIDS			
No	129 (48%)	69.4 ± 25.1	$t_{(266)} = 1.06$, $p = .290$
Yes	139 (52%)	72.5 ± 22.9	
Antiretroviral Therapy			
Not on treatment	77 (29%)	67.8 ± 26.2	$t_{(266)} = 1.42$, $p = .158$
On treatment	191 (71%)	72.3 ± 22.9	
Sleep Medication Use			
No	162 (60%)	74.0 ± 23.6	**$t_{(266)} = 2.51$, $p = .013$**
Yes	106 (40%)	66.5 ± 23.8	

	Mean ± *SD* or *n* (%)	**Cognitive Problems Mean ± *SD***	**Statistics**
Antidepressant Use (at therapeutic dose, $n = 264$)			
No	172 (65%)	73.1 ± 24.0	$t_{(262)} = 1.79$, $p = .075$
Yes	92 (35%)	67.6 ± 23.1	
Opiate Medication Use			
No	198 (74%)	71.4 ± 24.3	$t_{(266)} = 0.41$, $p = .684$
Yes	70 (26%)	70.0 ± 23.2	
Anemia ($n = 166$)			
No	116 (43.3)	72.0 ± 22.6	$t_{(164)} = 0.10$, $p = .918$
Yes	50 (18.7)	72.4 ± 25.7	
Body Mass Index	27 ± 5.6		$r = 0.051$, $p = .403$

Note. **Bolded** statistics indicate significant associations with self-reported cognitive problems ($p < .05$).

Table 2

Sleep and Fatigue Variables Associated with Cognitive Problems (n = 268)

Characteristics	Mean ± *SD* range, or *n* (%)	Cognitive Problems Mean ± *SD*	Association with Cognitive Problems
Objective Sleep (Actigraphy)			
Wake after sleep onset (WASO %)			
Mean ± *SD*	20.5 ± 14.7		$r = 0.007$, $p = .903$
Range	0.63–78.9		
< 10% WASO	79 (30%)	70.9 ± 23.0	$F_{(2,265)} = 0.112$, $p = .894$
10–29% WASO	127(47%)	70.5 ± 24.4	
≥ 30% WASO	62 (23%)	72.3 ± 24.7	
Total sleep time, hours (TST)			
Mean ± *SD*	6.2 ± 1.6		$r = 0.033$, $p = .589$
Range	1.3–11.4		
7–8 hours TST	49 (18%)	78.2 ± 19.1	**$t_{(87.7)} = 2.76$, $p = .007$**
< 7 or > 8 hours TST	219 (82%)	69.4 ± 24.7	
Subjective Sleep (PSQI)			
Global Sleep Quality Index			
Mean ± SD	7.25 ± 3.6		**$r = -0.378$, $p < .001$**
Range (0–21)	1–18		
≤ 5 (below clinical threshold)	98 (37%)	79.7 ± 21.6	**$t_{(219)} = 4.80$, $p < .001$**
> 5 (at or above threshold)	170 (63%)	66.0 ± 23.9	
Sleep Efficiency ($n = 254$)			
Mean ± *SD*	84.7 ± 14.9		**$r = 0.169$, $p = 007$**
Range	40–100		
< 70% sleep efficiency	40 (16%)	59.9 ± 28.2	**$F_{(3,250)} = 4.09$, $p = .007$**
70–79% sleep efficiency	39 (15%)	70.4 ± 19.0	
80–89% sleep efficiency	57 (22%)	73.9 ± 19.8	
≥ 90% sleep efficiency	118 (47%)	73.9 ± 24.4	
Sleep Latency, minutes ($n = 261$)			
Mean ± *SD*	25.4 ± 22.8		$r = -0.023$, $p = .715$
Range	0–180		
< 15 minutes latency	90 (35%)	74.2 ± 24.5	$F_{(2,258)} = 2.71$, $p = .069$
15–29 minutes latency	65 (25%)	65.6 ± 26.0	
≥ 30 minutes latency	106 (40%)	72.4 ± 20.7	
Sleep Duration, hours ($n = 264$)			
Mean ± SD	7.1 ± 1.5		**$r = 0.173$, $p = .005$**
Range	2.5–12		
7–8 hours	111 (41%)	74.8 ± 21.0	**$t_{(260)} = 2.26$, $p = .025$**

Characteristics	Mean ± *SD* range, or *n* (%)	Cognitive Problems Mean ± *SD*	Association with Cognitive Problems
< 7 or > 8 hours	157 (59%)	68.4 ± 25.6	
Subjective Sleep Quality (*n* = 267)			
Mean ± *SD*	1.06 ± 0.74		**$r = -0.274$, $p < .001$**
Range	0–3		
Sleep Disturbance (*n* = 268)			
Mean ± *SD*	10.1 ± 5.3		**$r = -0.386$, $p < .001$**
Range	0–27		
Daytime Dysfunction (*n* = 263)			
Mean ± *SD*	1.59 ± 1.3		**$r = -0.472$, $p < .001$**
Range	0–6		
Sleeping Medication Use (*n* = 268)			
Mean ± SD	0.88 ± 1.2		**$r = -0.130$, $p = .033$**
Range	0–3		
No	162 (60%)	74.0 ± 23.6	**$t_{(266)} = 2.51$, $p = .013$**
Yes	106 (40%)	66.5 ± 23.8	
Fatigue (LFS)			
Morning Fatigue			
Mean ± *SD*	3.4 ± 2.3		**$r = -0.356$, $p < .001$**
Range (0–10)	0–9.5		
Evening Fatigue			
Mean ± *SD*	5.1 ± 2.3		**$r = -0.210$, $p = .001$**
Range (0–10)	0–9.8		
Cognitive Problems (MOS)			
Mean ± *SD*	71.0 ± 24.0		
Median	76.7		
Range (0–100)	0–100		

Note. PSQI = Pittsburgh Sleep Quality Index; LFS = Lee Fatigue Scale; MOS = Medical Outcome Study; SD = standard deviation; **Bolded** statistics indicate significant associations with self-reported cognitive problems ($p < .05$).

Table 3

Pearson Correlation Matrix of Objective Measures of Sleep, Subjective Sleep Quality, Fatigue, and Cognitive Problems

	WASO	TST	PSQI	AM Fatigue	PM Fatigue
Sleep disruption (WASO)	-				
Sleep duration (TST)	−0.719**				
Subjective sleep quality (PSQI)	0.118	−0.115			
AM Fatigue	−0.125*	0.087	0.335**		
PM Fatigue	−0.140*	0.090	0.236**	0.665**	
Cognitive problems (MOS)	0.007	0.033	−0.378**	−0.356**	−0.210**

Note. WASO = wake after sleep onset; TST = total sleep time; PSQI = Pittsburgh Sleep Quality Index; AM = morning; PM = evening; MOS = Medical Outcome Study Cognitive Function Scale

* $p < .05$

$p < .01$.

Table 4

Multivariate Regression Model for Cognitive Problems ($R^2 = 0.247$, $p < .001$)

Characteristics	B	SE	95% CI	T statistic	*P* value	Δ in R^2
Step 1: Demographics						.034
Age	0.074	0.154	[−0.23 – 0.38]	0.48	.632	
Gender						
Male						
Female	−5.542	3.129	[−11.70 – 0.62]	−1.77	.078	
Transgender	−10.766	4.842	[−20.3 – −1.12]	−2.24	**.027**	
Education						
> high school						
≤ high school	−1.327	2.752	[−6.75 – 4.09]	−0.48	.630	
Step 2: Clinical Characteristics						.057
Sleep Medication Use						
No						
Yes	−0.103	2.878	[−5.77 – 5.56]	−0.04	.971	
Step 3: Objective Sleep Measures						.077
TST (actigraphy)						
7 – 8 hrs						
< 7 or > 8 hrs	−8.255	3.355	[−14.86 – 1.65]	−2.46	**.015**	
Step 4: Subjective Sleep Quality						.182
Sleep Quality (PSQI)	−1.758	0.403	[−2.55 – −0.96]	−4.36	< **.001**	
Step 5: Fatigue						.247
Morning Fatigue (LFS)	−2.905	0.612	[−4.11 – −1.70]	−4.75	< **.001**	

Note. B = unstandardized slope coefficient; *SE* = standard error; CI = confidence interval; TST = total sleep time; PSQI = Pittsburgh Sleep Quality Index; LFS = Lee Fatigue Scale; **Bolded** *p*-values represent significant associations with self-reported cognitive problems ($p < .05$).