Anxiety Sensitivity in Relation to Sleep Quality Among HIV-Infected Individuals

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Sleep disturbance is one of the most prevalent symptoms reported by HIV-infected individuals (Wheatley & Smith, 1994), with up to 73% reporting significant sleep disturbances (Rubinstein & Selwyn, 1998). Unlike some other symptoms associated with HIV that typically present during the initial phase of illness (e.g., fever, chills, muscle aches), sleep disturbance has been shown to be present over the course of the disease (Reid & Dwyer, 2005). This is particularly concerning as disturbed sleep has been associated with poorer antiretroviral (ART) medication adherence (Babson, Heinz, & Bonn-Miller, 2013), viral load (Saberi, Neilands, & Johnson, 2011), greater HIV symptom severity (Babson et al., 2013; Robbins, Phillips, Dudgeon, & Hand, 2004), and higher rates of negative psychological symptoms (Nokes & Kendrew, 2001).

While the prevalence and consequences of sleep disturbances among individuals with HIV have been established, relatively little work has investigated malleable factors that may confer greater risk of sleep disturbances for this population. One relevant factor in this area is anxiety sensitivity (AS), a cognitive vulnerability defined as the fear of anxiety, its relevant bodily sensations, and its potential negative social, physical, and mental consequences (Taylor et al., 2007). AS has unique relations to sleep disturbances and, among individuals with HIV, specifically, has been linked to greater physiological distress, anxiety, and depression symptoms (Gonzalez, Zvolensky, Parent, Grover, & Hickey, 2012; Gonzalez, Zvolensky, Solomon, & Miller, 2010), suicidality (Capron, Gonzalez, Parent, Zvolensky, & Schmidt, 2012), as well as self-reported HIV symptom severity (Leyro, Vujanovic, & Bonn-Miller, in press).

Unfortunately, there has been little work in terms of understanding whether greater AS might relate to decrements in sleep quality among individuals with HIV. Drawing from the literature more broadly, Vincent and Walker (2001) found that, in a sample of adults with chronic insomnia, AS was related to sleep-related impairment, with a trend relation between AS and frequency of medication use, after accounting for general worry and presence of Axis I psychopathology. Babson, Trainor, Bunaciu, and Feldner (2008) found that AS interacted with sleep anticipatory anxiety to predict sleep onset latency, after accounting for negative affect, gender, age, cannabis use, nicotine dependence, and alcohol use. In a similar investigation conducted among

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JOURNAL OF THE ASSOCIATION OF NURSES IN AIDS CARE, Vol. 25, No. 6, November/December 2014, 638-645
http://dx.doi.org/10.1016/j.jana.2014.02.002

individuals with panic disorder, Hoge et al. (2011) found that after accounting for relevant covariates including age, major depression, and panic disorder severity, individuals with elevated AS reported significantly greater latency to sleep. Taken together, these studies indicated that elevations in AS confer risk for greater sleep disturbances, although these associations appear nuanced in terms of particular aspects of sleep quality, with no research having sought to elucidate these relations for individuals with HIV.

Our study sought to explore the incremental association between AS and global sleep quality, as well as to determine differential associations between AS and a variety of facets that comprise global sleep quality, including perceived sleep quality, latency, duration, efficiency, disturbance, medication use, and daytime dysfunction in HIV-infected individuals receiving treatment at community clinics. We sought to explore AS in relation to global sleep impairment and specific components in order to explicate which aspects of sleep interference might be most relevant to AS. Such targeted examination will help provide a foundation for prospective work on AS and the etiology and maintenance of sleep pathology, with a long-term goal of guiding intervention development. Because AS serves to amplify fearful responses, it was hypothesized that AS would be associated with decrements in global sleep quality. In addition, we sought to conduct exploratory analyses on the relations between AS and each of the specific components of global sleep quality. Based on previous research that suggested that age, gender, ethnicity (Lichstein, Durrence, Riedel, Taylor, & Bush, 2004), and negative affect (Bower, Bylsma, Morris, & Rottenberg, 2010; Harvey, 2011) were related to sleep disturbance, these factors were examined as potential covariates. Given that participants were categorized based on their cannabis use, and due to the elevated prevalence of alcohol use, both of which may impact sleep disturbance (Krystal, 2012; Roehrs & Roth, 2001), these were also considered as potential covariates.

Methods

Our analyses were secondary to a larger study, which examined cannabis use in relation to HIV medication adherence (Bonn-Miller, Oser, Bucossi, & Trafton, 2014). From this sample, 136 individuals who completed requisite questionnaires were included in the current study. Inclusionary criteria involved being (a) at least 18 years old, (b) HIV infected, (c) currently prescribed at least one antiretroviral medication, and (d) undergoing treatment at an outpatient HIV clinic. As the parent study sought to examine cannabis use in relation to HIV medication adherence, participants fell into separate cannabis use categories such that approximately one third ($n = 40$) met *Diagnostic and Statistical Manual of Mental Disorders-IV (*DSM-IV; with the inclusion of withdrawal) criteria for current cannabis dependence, one third of the sample ($n = 47$) were nondependent cannabis users (use in the previous 30 days), and one third ($n = 49$) reported no cannabis use within the previous 6 months. Exclusionary criteria included (a) limited mental competency; (b) inability to provide informed, voluntary, written consent; (c) inability to speak and read English; or (d) suicidal ideation as determined by structured clinical interview.

Measures

Log-transformed viral load. Participants' viral loads (copies/mL), as determined by the most recent blood test, were obtained via a review of participants' medical records on file at their HIV clinics. Viral load was used as a reflection of participants' HIV status, burden of infection, and response to ART (U.S. Health Resources and Services Administration, 2012), and considered as a potential covariate given that research has indicated that viral load and disease burden impact sleep (Robbins et al., 2004; Saberi et al., 2011). Consistent with prior work (Mellors et al., 1997), viral load was log-transformed prior to analysis.

The structured clinical interview for DSM-IV axis I disorders-non-patient edition (SCID-I-N/P). The SCID-I-N/P (First, Spitzer, Gibbon, & Williams, 2002) is a well-established semi-structured interview used to determine diagnostic status of axis-I psychological disorders. Trained research assistants administered the SCID-I-N/P to assess for current suicidal ideation and axis-I psychopathology, including

cannabis use disorder status. All interviews were audio-recorded for review by the last author, a clinical psychologist, with no instances of disagreement.

The alcohol use disorders identification test (AUDIT). The AUDIT (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) is a 10-item valid and reliable self-report screening measure developed by the World Health Organization to identify individuals with alcohol problems, and it includes items that assess alcohol use frequency and quantity (e.g., *How often do you have a drink containing alcohol?*), as well as items used to assess abuse and dependence (e.g., *Have you or someone else been injured as a result of your drinking?*). The total score is derived from the sum of items 1 through 8 (0 = *never* to 4 = e.g., *daily/almost daily*) and items 9 and 10 scored as 0, 2, or 4. Because alcohol use may result in sleep disturbance (Krystal, 2012) in our study, the AUDIT total score was used to assess hazardous or harmful drinking (scores > 8; Cronbach's α = .87) and was examined as a potential covariate.

The positive and negative affect schedule (PANAS). The PANAS (Watson, Clark, & Tellegen, 1988) is comprised of 20 emotion words (e.g., *excited, distressed*) rated on a five-point Likert-type scale (1 = *very slightly or not at all* to 5 = *extremely*) by respondents based on how they have felt during the previous 2 weeks. Factor analysis of the 20 items indicates two global dimensions: positive affect (PANAS-PA) and negative affect subscales (PANAS-NA), with each demonstrating good internal consistency (Watson, 2000). Given empirical links between negative mood states (e.g., depression and anxiety) and sleep disturbance (Krystal, 2012; Robbins et al., 2004), the PANAS-NA was considered as a covariate to account for participants' general negative affect (Cronbach's α = .81).

The anxiety sensitivity index-3 (ASI-3). The ASI-3 (Taylor et al., 2007) is an 18-item self-report index of fear of anxiety and its potential consequences. Items are rated on a four-point Likert-type scale (0 = *very little* to 4 = *very much*), with higher scores indicating greater sensitivity and concern about anxiety. The ASI-3 was developed in order to improve upon the psychometric properties of the previously identified factors (physical, cognitive, and social) of the original index and has demonstrated good internal consistency, construct validity, and test-retest reliability. In our investigation, the total score was utilized (Cronbach's α = .95).

The pittsburgh sleep quality index (PSQI). The PSQI (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a 19-item self-report measure designed to assess previous-month sleep quality. Items are used to calculate seven component scores: subjective sleep quality (PSQI-quality; i.e., self-reported quality of sleep), sleep latency (PSQI-latency; i.e., amount of time to fall asleep), sleep duration (PSQI-duration; i.e., self-reported number of hours of sleep/night), habitual sleep efficiency (PSQI-efficiency; i.e., the amount of time spent asleep/the amount of time spent in bed), sleep disturbances (PSQI-sleep disturbance; i.e., awakenings during the night), using medication to sleep (PSQI-medication; i.e., use of prescription and over-the-counter medications used for the purposes of sleep), and daytime dysfunction (PSQI-daytime dysfunction; i.e., functional impairment during the day as a result of consequences of sleep loss). The sum of these components is used to calculate a global score. Psychometric evaluation of this index has indicated good internal consistency, test-retest reliability, and utility in both clinical and research settings. Global scores greater than 5 are indicative of clinical levels of insomnia. In our investigation, both the global score (Cronbach's α = .91) and its component scales were evaluated.

Procedure

Our investigation is a secondary analysis of a study investigating the impact of cannabis use on medication adherence (Bonn-Miller et al., 2014). Participants were recruited from local clinics and, if interested, contacted the laboratory for completion of a telephone screen to ensure basic inclusionary and exclusionary criteria; eligible participants were scheduled for an in-person session. Here, participants completed written informed consent, a diagnostic interview, and a battery of self-report questionnaires. In addition, all participants in the investigation provided permission for viral load results to be obtained

from recent medical records. The study session duration was approximately 2 hours, and participants were compensated $50 upon completion. The Stanford University Institutional Review Board (IRB) and Mills Peninsula IRB approved all study procedures.

Results

Descriptive Data and Correlations Among Theoretically Relevant Variables

Participants were 136 HIV-infected individuals (80.9% male; M_{age} = 47.75 years, SD = 8.95) recruited from four San Francisco Bay Area HIV clinics between 2010 and 2012. The sample average log-transformed viral load was 1.83 (SD = .71), which was consistent with that found among individuals undergoing treatment for HIV. In terms of ethnicity, 33.8% of participants identified as Black/Non-Hispanic, 33.8% as White/Caucasian, 10.3% as Black/Hispanic, 12.5% as Hispanic, 1.5% as Asian, and 8.1% as Other. The majority of participants reported graduating from high school or completing part of college (55.1%), with 15.4% acquiring 12 or fewer years of education, 18.4% graduating from a 2- or 4-year college, and 11.0% completing professional or graduate school. The majority of the sample reported they had never been married (48.1%); 22.2% were separated, divorced, or annulled; 22.2% were married or living with a partner; and 7.4% were widowed. On average, participants met criteria for 1.42 (SD = 1.56) DSM-IV Axis-I disorders, with 44.9% meeting criteria for an anxiety disorder and 18.4% for a mood disorder. In terms of alcohol use, 36.8% reported no current alcohol use, 25.0% reported drinking monthly or less, 19.1% reported drinking two to four times a month, 11.8% two to three times a week, and 7.4% four or more times a week. Of those who reported current alcohol use, most reported just one or two drinks per occasion (68.6%). On average, participants who reported drinking scored a 9.49 (SD = 7.81) on the AUDIT (Babor et al., 2001), consistent with hazardous or harmful use (Table 1).

First, zero-order correlations between theoretically relevant variables and our dependent variables (i.e., PSQI-global and subscale scores) were examined in order to determine model covariates. Pearson's correlations were used for continuous variables, including AS, PANAS-NA, age, log-transformed viral load, and total AUDIT, whereas analysis of variance was used for rank order and dichotomous variables, including cannabis group (dependent, nondependent, or nonuser), gender, education, and ethnicity. Negative affectivity was significantly and positively correlated with PSQI-global ($p < .01$), PSQI-quality ($p < .01$), PSQI-latency ($p < .05$), PSQI-disturbance ($p < .01$), and PSQI-daytime dysfunction ($p < .01$) scores. Total AUDIT score was significantly correlated with PSQI-quality ($p < .05$), PSQI-sleep disturbance ($p < .01$), and PSQI-daytime dysfunction ($p < .05$). Females reported significantly greater PSQI-global ($p < .05$) and PSQI-daytime dysfunction ($p < .05$) scores. Level of education was significantly correlated with PSQI-global ($p = .01$), PSQI-quality ($p < .05$), and PSQI-latency ($p < .01$). Ethnicity was significantly correlated with PSQI-global ($p < .05$) and PSQI-duration ($p < .05$), while log-transformed viral load and marital status were not significantly related to PSQI-global or its subscales. Despite lack of a relation to PSQI and its subscales, cannabis group status was included as a covariate as the parent study was specifically designed to examine differences in medication use based on cannabis use status, and participants were recruited as such (Bonn-Miller et al., 2014). Correlations among main predictors and PSQI global and its component scores indicated that AS was significantly and positively related to PSQI-global ($p < .01$) and six of the seven PSQI components (PSQI-quality, latency, duration, sleep disturbance, and daytime dysfunction, $p < .01$; PSQI-efficiency, $p < .05$).

Anxiety Sensitivity in Relation to Global Sleep Quality

A linear multiple regression analysis was first conducted to test the hypothesis of a relation between AS and PSQI-global, above and beyond selected covariates (Table 2). Although no covariates were significant predictors in the model, AS was found to be significantly incrementally associated with PSQI-global.

Table 1. Demographic Characteristics (N = 136)

Variable	% (n) or M (SD)
Gender	
Male	80.9% (n = 110)
Female	19.1% (n = 26)
Age	47.75 (8.95)
Log-transformed viral load[a]	1.83 (.71)
Ethnicity	
White/Caucasian	33.8% (n = 46)
Black/non-Hispanic	33.8% (n = 46)
Black/Hispanic	10.3% (n = 14)
Hispanic	12.5% (n =1 7)
Asian	1.5% (n = 2)
Other	8.1% (n = 11)
Education	
Less than high school	15.4% (n = 21)
High school or part of college	55.1% (n = 75)
Graduated from 2- or 4-year college	18.4% (n = 25)
Completed graduate or professional school	11.0% (n = 15)
Partner status (n = 135)	
Never married	48.1% (n = 65)
Separated/divorced/annulled	22.2% (n = 30)
Married or living with partner	22.2% (n = 30)
Widowed	7.4% (n = 10)
Axis I psychopathology diagnoses	1.4 (1.56)
Anxiety diagnosis	44.9% (n = 61)
Depression diagnosis	18.4% (n = 25)
Total AUDIT score[b]	9.49 (7.81)
Average drinks/occasion among drinkers	
Alcohol use	
None	36.8%
Monthly or less	25.0%
2–4 times a month	19.1%
2–3 times a week	11.8%
4+ times a week	7.4%

a. Log-transformed viral load (Mellors et al., 1997).
b. Alcohol Use Disorders Identification Test (Babor et al., 2001).

Anxiety Sensitivity in Relation to Component Sleep Quality Indices

Subsidiary linear multiple regressions separately examined the relations between AS and each of the seven PSQI component scores (Table 2). To correct for type 1 error associated with multiple predictors in the following six subsidiary analyses, a Bonferroni correction was applied to minimize error, resulting in a p-value threshold of .008 (.05/6 = .008). Results indicated that AS was significantly related to PSQI-quality and PSQI-duration, such that those with greater AS indicated poorer self-reported sleep quality and duration. AS was not associated with PSQI-latency, PSQI-efficiency, PSQI-sleep disturbance, or PSQI-daytime dysfunction.

Discussion

Disproportionately high rates of sleep disturbances in HIV-infected individuals are linked to a range of poor outcomes (e.g., poor ART adherence and greater psychological interferences; Babson et al., 2013; Nokes & Kendrew, 2001; Phillips et al., 2005), yet little work has investigated the relation between malleable psychological vulnerabilities and sleep disturbances in this population. To fill this gap in the literature, our investigation sought to examine AS in relation to sleep disturbance in individuals with HIV. First, findings indicated that HIV-infected individuals higher in AS reported greater global sleep disturbance, providing novel evidence for the role of AS in terms of general sleep disturbances for those with HIV. Additionally, the observed association was evident above and beyond general negative affectivity, as well as a number of other theoretically and empirically relevant factors (i.e., cannabis use, gender, education, and ethnicity). These data add to previous work linking AS to greater psychological disturbance and symptoms in individuals infected with HIV (Capron et al., 2012; Gonzalez et al., 2012) by suggesting that AS was uniquely associated with sleep difficulties in this population.

Exploratory analyses revealed significant associations between AS and perceived sleep quality and self-reported sleep duration, after accounting for theoretically and empirically relevant covariates. Interestingly, AS was not significantly related to using medications to sleep (Vincent & Walker, 2001) or sleep onset latency (Babson et al., 2008; Hoge et al., 2011), suggesting that these previously observed associations may not be relevant to populations with HIV. Alternatively, it is possible that these differing findings were related to differences in sample characteristics, including elevations in psychological comorbidity as well as differences in measurement method. For example, research by Vincent and Walker (2001) recruited individuals with a current diagnosis of insomnia and

Table 2. Summary of Hierarchical Regression Analyses

	ΔR^2	*t*	β	sr^2	*p*-Value
Criterion variable: PSQI Global[a]					
Step 1	.16				<.001
Cannabis group[b]		1.10	.09	.01	.28
PANAS-NA[c]		3.61	.30	.08	<.001
Gender[d]		1.29	.11	.01	.20
Education[e]		−1.35	−.11	.01	.18
Race/ethnicity[f]		−.30	−.03	.00	.76
Step 2	.09				.001
AS[g]		3.90	.36	.09	<.001
Criterion variable: PSQI sleep quality[a]					
Step 1	.15				<.001
Cannabis group[b]		−.73	−.06	.00	.47
PANAS-NA[c]		3.51	.30	.08	.001
AUDIT[h]		1.23	.11	.01	.22
Education[e]		−1.93	−.16	.02	.06
Step 2	.06				<.001
AS[g]		3.17	.30	.06	.002
Criterion variable: PSQI latency to sleep[a]					
Step 1	.07				.019
Cannabis Group[b]		.24	.02	.00	.81
PANAS-NA[c]		2.47	.21	.04	.015
Education[e]		−1.47	−.13	.02	.14
Step 2	.02				.01
AS[g]		1.86	.19	.02	.06
Criterion variable: PSQI sleep duration[a]					
Step 1	.06				.08
Cannabis group[b]		.81	.07	.00	.42
PANAS-NA[c]		1.63	.14	.02	.11
Gender[d]		1.76	.15	.02	.08
Race/ethnicity[f]		.75	.06	.00	.46
Step 2	.05				.009
AS[g]		2.66	.26	.05	.009
Criterion variable: PSQI sleep efficiency[a]					
Step 1	.02				.08
Cannabis group[b]		1.75	.15	.02	.08
Step 2	.03				.021
AS[g]		2.19	.18	.03	.03
Criterion variable: PSQI sleep disturbance[a]					
Step 1	.18				<.001
Cannabis group[b]		1.38	.11	.01	.17
PANAS-NA[c]		3.98	.32	.10	<.001
AUDIT[h]		1.69	.14	.02	.09
Step 2	.03				<.001
AS[g]		2.05	.19	.03	.042
Criterion variable: PSQI daytime dysfunction[a]					
Step 1	.26				<.001
Cannabis group[c]		.04	.00	.00	.97
PANAS-NA[c]		5.50	.44	.19	<.001
Gender[d]		2.08	.16	.02	.04
AUDIT[h]		1.13	.09	.01	.26
Step 2	.01				<.001
AS[g]		1.38	.12	.01	.17

Note: PSQI = pittsburgh sleep quality Index; PANAS-NA = positive and negative affect schedule – negative affect; AS = anxiety sensitivity; AUDIT = alcohol use disorders identification test. $N = 136$; Significance for six subsidiary PSQI subscale analyses based on $p < .008$, following Bonferroni correction number of models (6/.05 = .008).

a. PSQI (Global Score and subscales; Buysse et al., 1989).

b. Cannabis group (1 = No use; 2 = Nondependent; 3 = Dependent).

c. PANAS (Watson et al., 1988).

d. Gender (1 = male; 2 = female).

e. Education (1 = Less than high school; 2 = high school or part college; 3 = graduated from 2- or 4-year college; 4 = completed graduate or professional school).

f. Race/ethnicity (1 = White/Caucasian; 2 = Black/Non-Hispanic; 3 = Black/Hispanic; 4 = Hispanic; 5 = Asian or "Other").

g. AS (Anxiety Sensitivity Index-3; Taylor et al., 2007).

h. AUDIT (Babor et al., 2001).

measured medication use in terms of past-month frequency, whereas using medication to help with sleep in our investigation was rated on a four-point scale. In terms of sleep latency, Hoge et al. (2011) examined the relation between AS and sleep latency in individuals with panic disorder, a group known to experience markedly high AS and over-attention to physiological symptoms and worry about physiological consequences of anxiety.

Notably, both perceived sleep quality and duration were indexed with a single item; therefore, these findings should be interpreted with some caution. For example, a rating of overall perceived sleep quality provides little descriptive information to aid in the understanding of how AS theoretically impacts sleep quality. In addition, there were limitations to self-report data, particularly among those with sleep disturbances, highlighting the need for objective measures of sleep, such as actigraphy and polysomnography (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008), that may help us more accurately index and understand the role of AS in relation to

insomnia in this population. Also, our study did not gather comprehensive information regarding possible use of sleep medication; therefore, we were unable to deduce the extent to which current participants were receiving pharmacological interventions for sleep disturbance. If a substantial portion of participants were indeed receiving pharmacological interventions for sleep, this may have limited our ability to detect a relation between AS and PSQI scales; however, it is notable that no relation was observed between AS and use of medication to sleep. Further, due to the cross-sectional nature of the study, determining whether AS served as a risk factor, maintenance factor, or both, in the context of sleep quality in individuals with HIV, remained unclear. Future research within this area should seek to examine the relation between AS and sleep disturbances prospectively.

Despite these limitations, our findings suggest the clinical utility of assessing AS among individuals with HIV. Health professionals across settings would benefit from such efforts by identifying individuals with HIV who are at greater risk for sleep disturbance and subsequently aiding in the appropriate allocation of resources toward these individuals. Beyond determining those at greatest risk, findings suggest that interventions geared toward reducing AS (Keough & Schmidt, 2012) may be beneficial in terms of improving sleep quality and associated outcomes for individuals with HIV.

Disclosures

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

Acknowledgments

This research was supported, in part, by the following: A California HIV/AIDS Research Program IDEA Award #163836 (Bonn-Miller), a VA Clinical Science Research and Development (CSR&D) Career Development Award-2 (Bonn-Miller), a T32 (DA007250-19) awarded to Dr. Leyro, and Health Services Research and Development service funds provided to Dr. Babson. The expressed views do not necessarily represent those of the Department of Veterans Affairs.

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