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Assessing Sleep in Opioid Dependence: A Comparison of Subjective Ratings, Sleep Diaries, and Home Polysomnography in Methadone Maintenance Patients

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Abstract

Objectives—Comparisons of subjective and objective sleep measures have shown discrepancies between reported sleep and polysomnography (PSG) in non-drug dependent individuals with and without insomnia. Sleep may affect behavioral and physiologic aspects of drug abuse and dependence; patients in methadone maintenance therapy (MMT) for opioid dependence frequently report sleep problems. Whether subjective sleep reflects objective sleep in MMT patients is unknown. We undertook these analyses to establish the correlations among subjective and objective sleep measures in MMT patients.

Methods—We compared one week of daily sleep diaries, one night of home PSG, a questionnaire completed the morning after PSG, and the Pittsburgh Sleep Quality Inventory (PSQI) as well as demographics and drug use measures in 62 MMT patients with disturbed sleep (PSQI score > 5).

Results—Subjective and objective sleep durations were similar in this sample; average sleep times for the diary, morning questionnaire, and PSG were 340, 323, and 332 minutes, respectively. Average diary sleep time, subjective ratings of feeling rested, and PSG sleep efficiency were

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Contributors

Michael D. Stein designed the study. Michael D. Stein and Richard P. Millman wrote the protocol. Megan E. Kurth managed participant recruitment and data collection. Richard P. Corso recruited participants and collected data. Authors Stein, Millman, Kurth, Anderson, and Sharkey planned the data analyses. Bradley J. Anderson performed the statistical analyses. Katherine M. Sharkey wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest

No conflict declared.

correlated significantly with PSQI score. Age was inversely correlated with PSG sleep time. Participants whose urine toxicology showed benzodiazapine use reported significantly longer sleep times on the morning questionnaire.

Conclusions—Objective sleep measures confirm subjective measures in MMT patients with disturbed sleep. The high prevalence of sleep complaints in this population likely reflects pathology rather than sleep misperception. Both objective and subjective measures are useful in research and clinical settings for assessing sleep in opioid-dependent patients.

Keywords

methadone; opioid dependence; sleep; polysomnography; PSQI; sleep diaries

1. Introduction

Sleep may impact drug use, treatment compliance, intervention efficacy, and relapse risk through behavioral and physiologic mechanisms. A role for sleep disturbance in addiction has been found in cocaine users (Morgan et al., 2006; Morgan et al., 2010), methadone patients (Stein et al., 2004; Peles et al., 2006; Kurth et al., 2009; Sharkey et al., 2009; Trksak et al., 2010), and alcohol dependent patients (Brower et al., 1998; Conroy et al., 2006). Among alcohol dependent patients in early recovery, for example, sleep disturbances and perceived sleep disruption are related to future alcohol use (Brower et al., 1998; Conroy et al., 2006).

Patients in methadone maintenance therapy (MMT) for opioid dependence frequently report sleep complaints (Oyefeso et al., 1997; Stein et al., 2004; Peles et al., 2006). One potential pathway to sleep disruption in MMT patients is opioid-induced reduction of the nucleoside adenosine in the basal forebrain (Nelson et al., 2009). The notion that reduced adenosine – a neurochemical modulator of the homeostatic drive for sleep – may be responsible for sleep disturbances in MMT patients is further supported by the observation that MMT patients fail to show typical recovery responses after a sleep-deprivation challenge (Trksak et al., 2010). Comorbid psychiatric disorders, chronic pain, and other drug use may also contribute to sleep complaints in MMT patients (Stein et al., 2004; Peles et al., 2006).

Comparisons of subjective and objective sleep measures in non-drug dependent individuals with and without insomnia have shown that self-reported sleep can differ substantially from physiologic recordings (Carskadon et al., 1976; Spinweber et al., 1985; Hauri and Wisbey, 1992; Silva et al., 2007). Whether subjective sleep complaints reflect objective sleep measures in MMT patients is unknown. In order to establish associations between subjective and objective sleep measures in MMT patients, we compared one week of sleep diaries to one night of polysomnography (PSG), a morning questionnaire following PSG, and the Pittsburgh Sleep Quality Inventory (PSQI).

2. Methods

2.1. Participants

As part of a clinical trial of a pharmacological insomnia treatment, we recruited 137 patients from 8 MMT clinics in Rhode Island from 2006 to 2009 (see Kurth et al., 2009)for details).

Inclusion criteria were: insomnia (PSQI > 5 at screening; Buysse et al., 1989), intent to continue MMT for 6 months, fluency in English, and stable housing. Exclusion criteria were: psychotic symptoms, diagnosis of bipolar disorder, schizophrenia, schizoaffective or schizophreniform disorder, trazodone use in the past month, pregnancy, and chronic medical illness. These analyses included 62 participants who were enrolled in MMT for ≥ 3 months, had completed at least one PSG night followed by a morning questionnaire, and had ≥ 3 days of sleep diaries during the week before PSG. PSG and sleep diaries were performed prior to medication assignment in the clinical trial and within 3 weeks of screening.

The study was approved by the Rhode Island Hospital and Butler Hospital Institutional Review Boards. Participants provided informed consent and were paid for participation.

2.2. Sleep Diaries

Participants completed a daily morning sleep diary during the week preceding PSG in which they recorded bedtime, time to fall asleep, number of awakenings, time awake during the night, wake up time, and a subjective measure of "feeling rested." *Diary time in bed* was calculated as the duration between bedtime and wake up time. *Diary total sleep time (TST)* was calculated by subtracting sleep latency and time awake during the night from *Diary time in bed*.

Diary sleep efficiency was calculated by dividing *Diary TST* by *Diary time in bed* x 100. Each sleep measure was averaged over the reported days. Most participants had 7 days of complete diary data; the average number of completed diary days was 6.2±1.2 days. We included participants with 3–7 diary days because sleep diary analyses in other populations indicate that reliable sleep estimates can be obtained with ≥ 3 days of data (Thomas and Burr, 2009).

2.3. Polysomnography and Morning Questionnaire

PSG recordings were made using portable recorders (Compumedics, Charlotte, NC, USA) on one or two consecutive nights. When two nights were completed, we used data from the longer PSG night. Researchers set up the study in the participant's home before his or her usual bedtime on the evening of PSG. No participant had behavior suggesting acute intoxication on the PSG night.

Objective sleep was measured using standard PSG techniques as previously described (Kurth et al., 2009; Sharkey et al., 2009; Sharkey et al., 2010) including electroencephalography, electrooculography, and electromyography. Respiration was monitored with nasal/oral airflow, nasal pressure transducers, pulse oximetry, and intercostal and abdominal respiration belts. EKG was monitored with electrodes on the chest. Researchers started the recordings and viewed signals for good quality before leaving participants' homes; they returned the following morning to collect equipment and administer the morning questionnaire, on which participants reported bedtime, wake up time, an estimate of TST, and number of awakenings.

PSG was scored in 30-second epochs according to Rechtschaffen and Kales criteria (Rechtschaffen and Kales, 1968) by a trained scorer who maintained > 90% concordance with a second trained scorer. The following measures were derived: *Sleep period time*, defined as the interval between the first and last epoch scored as sleep; minutes of total sleep time (TST); *Sleep efficiency*, calculated by dividing TST by sleep period time x 100; *Apnea/Hypopnea index* (number of apneas and hypopneas per hour of sleep); and *Arousal index* (number of electroencephalographic arousals per hour of sleep).

2.4. Statistical Analysis

Data were analyzed using Stata software version 10.1 (StataCorp, College Station, TX, USA). Means, counts, and percentages are reported to summarize the data. We used Spearman rank-order correlations to test associations between subjective and objective sleep measures as well as demographics and drug measures including methadone dose, duration of MMT enrollment, and urinalysis-confirmed use of drugs other than opioids. We used repeated measures ANOVA to compare subjective and objective TST. Alpha $< .05$ was considered statistically-significant.

3. Results

The 62 participants had a mean age of 39.2±8.3 years (range 21–56), and included 38 women and 54 non-Hispanic Caucasian participants. Median MMT enrollment duration was 13 months. Methadone dose ranged from 21 mg to 285 mg with a mean of 107.9±51.7 mg (median = 100 mg). Of those with valid urine drug tests on the PSG night (n = 55), we observed the following rates of drug use: benzodiazepines: 41.8% (n=23); cocaine: 27.8% (n=15); tetrahydrocannabinoids: 20.0% (n=11), and opiates: 14.8% (n=8). Average TST objectively recorded with PSG was 332±131 minutes. Participants reported an average sleep time of 323±99 minutes on the morning questionnaire following PSG and an average of 340±129 minutes on the sleep diaries completed the week prior to PSG. Sleep times did not different significantly among the subjective and objective measures ($F_{2, 218} = 1.93$, p=.15).

Objective sleep duration was significantly correlated with age (r=−.21, p<.05), with older participants having shorter PSG sleep times. Benzodiazepine use was significantly correlated with sleep time reported on the morning questionnaire (r=.19, p < .05), but was not related to PSG TST. Gender, MMT treatment duration, methadone dose, and other drug use were not correlated with any subjective or objective sleep duration measure.

Spearman rank-order correlations among sleep measures are shown in Table 1. *Diary time in bed*, *Diary TST*, and *Feeling rested* were correlated significantly with PSQI score, indicating that those who reported less time in bed, shorter TST, and rated themselves as less rested had higher sleep disturbance scores. PSQI score was not related to diary bedtime, wake time, number of awakenings, duration of awakenings, or sleep efficiency.

Several measures from the sleep diaries were related to objective PSG measures. *PSG TST* correlated significantly with *Diary time in bed*, *Diary TST,* and *Average Diary Bed Time*, with earlier reported bedtimes associated with longer PSG sleep times. *Diary sleep efficiency* was correlated significantly with *PSG sleep efficiency*, and with *PSG Arousal index*. Participants' reports of sleep disturbance on the PSQI were corroborated with objective sleep disturbance measured with PSG. Higher PSQI scores were associated significantly with lower PSG sleep efficiencies and higher percent time awake on PSG. PSQI scores were not associated with apnea/hypopnea index or arousal index.

4. Discussion

Most patients in MMT for opioid dependence report sleep difficulties, but no previous study has assessed whether subjective complaints of sleep disruption in MMT patients are correlated with objective sleep disturbance. Our data comparing PSG sleep with a morning sleep questionnaire demonstrate that MMT patients are reliable in reporting their sleep duration within a short time frame. In addition, this short-term consistency is reflected in sleep reported at other time points. Subjective sleep measured with daily sleep diaries and a PSQI rating of prior-month sleep difficulties were associated significantly with each other and with objective sleep measured using the gold-standard, PSG. These data indicate that MMT patients' subjective ratings reflect the duration and quality of their sleep. Moreover, the results indicate that subjective ratings to evaluate sleep in MMT patients can be useful in both research and clinical settings.

We examined demographic and drug use parameters to determine whether these factors were correlated with subjective or objective sleep measures. As has been shown in other samples, older age was associated with shorter PSG sleep duration (Ohayon et al., 2004). Duration of MMT, methadone dose, and use of drugs other than benzodiazepines were not correlated with PSG-measured sleep. Benzodiazepine use was associated with longer sleep time estimates on the morning questionnaire, paralleling findings of studies of hypnotic medications in insomnia patients (Hedner et al., 2000).

The association of objective and subjective sleep measures has been studied in other populations. Analyses of subjective versus objective sleep in middle-aged community-dwelling adults found that subjective reports of TST were higher than sleep times measured with home PSG (Silva et al., 2007). When insomnia patients were evaluated with in-laboratory PSG, they usually underestimated TST and over-estimated the time it took to fall asleep, although subjective and objective measures were correlated (Carskadon et al., 1976). In chronic cocaine users undergoing acute withdrawal, Morgan and colleagues (2006) found a dissociation of subjective and objective sleep measures. Their PSG findings showed a worsening of sleep parameters over 3 weeks of cocaine abstinence with a concomitant improvement in subjective sleep ratings. Conroy et al. (2006) found that recovering alcohol-dependent patients subjectively estimated PSG TST accurately, but underestimated wakefulness during the night, similar to patients with insomnia (Carskadon et al., 1976). Compared to other populations, our MMT patients were reliable in estimating their sleep times compared with PSG, and their sleep diaries for the week preceding PSG indicate that their usual self-reported sleep behavior was similar to the PSG night. Furthermore, objective and subjective sleep measures were significantly correlated with complaints of poor sleep on the PSQI, which assessed sleep during the prior month.

Study participation was limited to those reporting sleep disturbance, who represent > 80% of MMT patients (Stein et al., 2004). On average, participants obtained < 6 hours of sleep by all measures studied. These short sleep durations represent sleep restriction that would be expected to manifest in daytime impairment (Balkin et al., 2008). The reasons for these relatively short sleep times in MMT patients are unknown, and the association of sleep duration to daytime pathology has not been studied in opioid dependent patients. MMT patients use depressant drugs (e.g., benzodiazepines or other opioids) to facilitate sleep (Li et al., 2010; Stein et al., 2004), which could precipitate relapse. We speculate that shortened sleep might impair engagement with treatment leading to continued drug use or relapse and that daytime sleepiness could limit employment options for MMT patients. The clinical implication of our findings is that symptoms of insomnia in individual MMT patients merit investigation and treatment. In a research setting, choice of sleep measures may be tailored to specific scientific question and study context.

In conclusion, the present study establishes a correlation between subjective ‘past-month’ sleep complaints, sleep diaries, and PSG in patients receiving MMT for opioid dependence. Further research is needed to determine what interventions are most effective at improving sleep in MMT patients, and whether improved sleep results in better drug treatment outcomes.

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Table 1

Spearman rank-order correlations among objective (PSG) and subjective (morning questionnaire, daily sleep diaries, and PSQI) sleep measures.

	MORNING QUESTIONNAIRE		AVERAGE DAILY SLEEP DIARY MEASURES							PSQI SCORE
	Hours of Sleep	**Number of Awakenings**	**Time in Bed**	**Bed Time**	**Wake Time**	**Sleep Time (TST)**	**Time Awake**	**Rested Rating**	**Sleep Efficiency**	
PSG MEASURE										
Sleep Period Time	0.25	0.15	.33**	−.30*	.33**	.35**	0.17	−0.21	−0.02	0.09
Total Sleep Time	.37**	0.01	.33**	−.35**	0.23	.34**	0.1	−0.14	0.09	0.08
Sleep Efficiency	.35**	−.42**	0.19	−0.11	−0.03	0.07	−0.2	0.1	.26*	−.32*
Apnea/Hypopnea Index	0	0.13	−0.12	−0.15	−0.16	−0.13	0.17	−0.1	−0.19	0.13
Arousal Index	−0.15	0.01	−0.24	0.08	−0.11	−0.22	.27*	−0.14	−.35**	0.17
MORNING QUESTIONNAIRE										
Hours of Sleep			.42**	−.33**	0.24	.32*	−0.07	0.16	.26*	
Number of Awakenings			−0.09	−0.03	−0.1	−0.14	0.21	− 40**	−0.19	
PSQI SCORE	−0.15	.25*	−.29*	0.08	−0.2	−.29*	0.21	−.26*	−0.21	

* $p < .05$,

** $p < .01$