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Home Polysomnography in Methadone Maintenance Patients with Subjective Sleep Complaints

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Abstract

Objective—Most patients in methadone maintenance treatment (MMT) complain of poor sleep which is potentially linked to relapse, yet few studies have examined their sleep using polysomnography (PSG), and none to our knowledge have employed home PSG. Standard sleep laboratory research protocols often require two consecutive PSG nights because of inter-night variability in sleep attributed to first-night adaptation to a novel sleep environment and recording procedures. The purpose of this study was to assess the stability of sleep measures across two consecutive nights of home PSG in opioid-dependent MMT patients.

Methods—Home PSG was performed in 50 MMT patients with subjective sleep complaints. Participants were 54% female and 82% white with mean age = 36.8 years, median methadone dose = 100 mg/day, and median MMT duration = 286 days.

Results—Thirty-six participants completed two consecutive nights of at-home PSG and 14 completed one. For the former group, no differences in sleep measures were found across recordings. The one-night group had significantly less total sleep time, Stage 2 sleep, REM sleep, and shorter REM latency than the two-night group.

Conclusions—Home PSG is a viable method for recording sleep in opioid-dependent MMT patients, and was stable across consecutive nights of study. Two nights of home PSG for MMT patients, therefore, are not necessarily required and confidence in the reliability of data from one night of recording can be assumed. Excluding MMT research participants with only one PSG may exclude patients with the worst sleep – precisely the group that most warrants investigation.

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Keywords

sleep; methadone; opioid dependence; polysomnography; home monitoring

Introduction

Opiate dependence is a serious public health concern, with prevalence estimates ranging from 0.5–0.7% (1). Costs of opiate dependence including medical care, lost productivity, crime, and social welfare were estimated at \$21.9 billion in the United States in 1996 (2). Methadone maintenance therapy (MMT) is the mainstay treatment for opiate dependence and has been shown to reduce mortality, HIV risk behavior, and levels of crime (3). Nevertheless, discontinuation of MMT and continued use of opiates pose challenges to the treatment of patients with opiate dependence.

Previous work has documented subjective sleep disturbance in 75–84% of patients in methadone maintenance treatment (4, 5). In these studies, symptoms of depression and anxiety, greater nicotine dependence, benzodiazepine use, bodily pain, and unemployment were associated with increased subjective sleep complaints. It is unknown, however, whether sleep problems in MMT patients play a role in whether patients remain in treatment or resume using illicit drugs.

Despite the high prevalence of sleep complaints in this population, few studies have examined sleep in MMT patients using polysomnography. Previous laboratory investigations of sleep in patients taking methadone have demonstrated disrupted sleep, including increased Stage 2 sleep and decreased REM sleep compared to age-matched controls (6–8). Lower sleep efficiency and slow wave sleep (SWS) percent have also been observed (6). Variability in sleep parameters from night-to-night, however, has not been studied polysomnographically in MMT patients. Nor, to our knowledge, has at-home polysomnography been reported in MMT patients.

Unattended home polysomnography is becoming a more common method of measuring sleep. Its utility is evident in large research cohorts, for instance in the Sleep Heart Health Study (9–11), and in research populations that may be more logistically challenging to study in the sleep laboratory, including the elderly (12) and those with mental illness (13). MMT patients comprise a potentially challenging group to study, as do many other individuals with severe substance use disorders. Therefore, simplifying study procedures to alleviate participant burden in patients with substance use disorders is worthwhile, if scientific integrity is not compromised for the purposes of that study.

In general, it is standard procedure in sleep research involving polysomnography (PSG) to obtain two consecutive nights of recordings because of the possibility of inter-night variability as participants adapt to novel sleeping conditions. Changes in sleep quality and architecture attributed to adaptation to polysomnography – sometimes termed the “first-night effect” on sleep (14) – include alterations in duration and distribution of sleep stages, prolonged latencies to REM and slow wave sleep (SWS), increased sleep fragmentation, and changes in reported dream content. Proposed origins of the first-night effect include

unfamiliarity with a novel sleep environment, discomfort and decreased mobility related to the equipment used in polysomnography, and psychological distress due to being observed during sleep recordings (15). The role of environmental familiarity in manifesting as a first-night effect has been examined using home polysomnography. Although some studies did not show first night effects when polysomnography was performed in the home (16), other investigations have shown inter-night variability even with home PSG (12, 15, 17).

The present study employed unattended at-home polysomnography to study sleep in opioid-dependent patients in MMT. Its overall purpose was to analyze the stability of measured sleep variables across two consecutive nights of recordings. If statistically different results were found, then we reasoned that the standard two-night protocol was justified, and that data obtained from participants who completed only one night of PSG might misrepresent a patient's usual sleep pattern. If, on the other hand, sleep recordings produced data that were generally stable across nights, then one night of recording might suffice for most purposes, and additional study burden on participants could be prevented. Participants in this study were expected to complete two consecutive nights of PSG, but not all of them did. Accordingly, our specific aims were: (1) to investigate the stability of sleep measures across two consecutive nights of recordings; and (2) to examine the correlates of completing both nights of recordings, as was expected in our study protocol.

Methods

Participants were recruited from 8 MMT clinics in the Providence, Rhode Island metropolitan area from January 2006 to October 2007 as part of an ongoing clinical trial to test a pharmacological treatment for insomnia.

Inclusion criteria were: subjective sleep disturbance – defined as a score > 5 on the Pittsburgh Sleep Quality Index (PSQI) (18), stable housing, plans to continue MMT for at least 6 months, and proficiency in written and spoken English. Exclusion criteria were: current DSM-IV diagnosis of substance dependence other than nicotine, bipolar disorder, schizophrenia, schizoaffective disorder, schizophreniform disorder, major depression, trazodone use in the previous 30 days, pregnancy, ischemic heart disease, known obstructive sleep apnea, poorly controlled diabetes mellitus, poorly controlled chronic obstructive pulmonary disease/emphysema, and inability to identify two contact persons.

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

Polysomnographic recordings were made using portable Siesta or Safiro units (Compumedics, Charlotte, NC, USA) on two consecutive nights, Monday–Thursday. On the evening of a home study, two research assistants went to the home of the participant 1–3 hours before the participant's reported usual bedtime. Participants gave a urine sample for toxicology screening and performed a breathalyzer test. The research assistants were instructed not to proceed with participants whose behavior suggested acute intoxication that would preclude completion of the protocol.

Sleep was measured using electroencephalography recorded from C3 and C4 referenced to the contralateral mastoids, electrooculography from ROC and LOC, and electromyography from submental surface electrodes. Respiration was monitored with nasal/oral thermocouples or thermistors, nasal pressure transducers, pulse oximetry, and surface intercostal and abdominal piezo crystal respiration belts. EKG was monitored with surface electrodes on the chest and side. Research assistants started the recordings and viewed polysomnographic signals for good quality before leaving the participants' homes. Research assistants returned to collect the equipment the following morning.

Polysomnography (PSG) was scored in 30-second epochs according to Rechtschaffen and Kales criteria (19) by a trained scorer who maintained > 90% concordance with a second trained scorer. Sleep period time was defined as the interval between the first epoch scored as sleep and the last epoch scored as sleep. Sleep efficiency was calculated by dividing total sleep time by sleep period time x 100. Sleep latency was not calculated because participants' estimates of lights out time were considered unreliable. Therefore, sleep latency is not included in the calculation of sleep efficiency.

Statistical Analysis

Data were analyzed using Stata software version 9.2 (StataCorp, College Station, TX, USA). Based on criteria set in the Sleep Heart Health Study (9), we excluded recording nights that contained less than 4 hours of contiguous data and included only participants who completed at least one night with a sleep period time ≥ 4 hours. To examine variability in recordings among participants who completed two consecutive PSG nights, we used non-independent t-tests to analyze night-to-night differences in standard sleep variables reflecting sleep continuity, sleep architecture, and REM sleep parameters. To examine correlates of completing two nights of PSG, differences in demographic, clinical, and sleep variables between participants who completed one night versus two nights of recordings were tested using chi-square tests for categorical variables and independent samples t-tests for differences in means. Because sample sizes were small we also tested between-group differences using the nonparametric Wilcoxon rank-sum test; results were consistent with those we report.

Results

Thirty-six (72%) MMT patients completed two nights of PSG and 14 (28%) completed one night. The 50 participants were 54% female and 82% white with a mean age of 36.8 years (range = 22–52 years). Mean ± SD PSQI score was 12.6 ± 2.9 . The overall median methadone dose was 100 mg daily (range 25–310 mg) and the median duration of MMT was 286 days (n=39 available). Sixty-two percent of participants had positive toxicological tests for drugs other than methadone (benzodiazepines, tetrahydrocannabinol, cocaine, and/or opiates other than methadone). Eleven of 14 participants with only one PSG were observed on night 1 and three of 14 had the valid recording on night 2. The reasons for having only one PSG were: contiguous sleep recording < 4 hours (n=7), equipment failure (n=5), and participant not home/not available for the study (n=2). The 36 participants with two nights

of PSG did not differ significantly from the 14 with one valid PSG night in sex, race, age, PSQI score, methadone dose, length of methadone treatment, or illicit drug use.

Sleep variable data for participants who completed two nights of home PSG are shown in Table 1. On average, participants had low total sleep time and sleep efficiency, low percent REM sleep, and long wake after sleep onset relative to published normative values (20, 21). There were no significant differences ($p < .05$) between night 1 and night 2 in any sleep measures.

Table 2 shows sleep variable data by night completion status. Compared to participants who completed two nights of PSG recording, those who completed one night had significantly shorter sleep period time ($t=-3.82$, $df=48$, $p=0.0004$), shorter total sleep time ($t=-3.59$, $df=48$, $p=0.0008$), fewer minutes of Stage 2 sleep ($t=-2.79$, $df=48$, $p=0.008$), fewer minutes of REM sleep ($t=-2.91$, $df=48$, $p=0.005$), and shorter REM latency ($t=-2.35$, $df=48$, $p=0.02$).

Discussion

This study had two major findings. First, no significant differences in sleep measures were found across two consecutive nights of baseline at-home polysomnography in opioid-dependent MMT patients. Second, patients completing only one night of PSG had worse sleep than patients completing two nights, which was neither attributable to demographic differences between the two groups, nor to their daily dose of methadone, use of illicit drugs, or severity of subjective sleep disturbance.

Although we are not aware of previous investigations of home-PSG in opiate-dependent patients, in-laboratory PSG has been studied in opioid-dependent patients taking methadone. For instance, Teichtahl and colleagues (6) studied 10 MMT patients with a median methadone dose of 85 mg, and observed that patients had significantly less SWS and REM sleep, increased Stage 2 sleep, and increased total wake time compared to age-matched controls. A larger study of 50 MMT patients also documented less REM sleep in patients compared to controls, as well as increased Stage 2 sleep and decreased Stage 1 sleep, but did not demonstrate reductions in SWS (7). In older studies of sleep in patients taking methadone, Orr and Stahl (22) found an increase in Stage 1 percent and decrease in SWS percent and Kay (23) linked opiate use with increased REM latency. In our study of MMT patients, home PSG recordings documented abnormalities in similar sleep parameters compared to normal adults in this age range (20, 21), including lower total sleep time, lower REM sleep time, and higher wake after sleep onset. These findings corroborate our participants' subjective sleep complaints and also replicate other published sleep data for methadone-treated patients. It is likely that use of drugs other than methadone in over 50% of participants contributed to observed sleep abnormalities. Further studies are needed to determine whether disturbed sleep in MMT patients predicts relapse as has been observed in other substance-dependent populations, e.g., alcohol dependence (24).

Previous studies of between-night differences in other study populations have highlighted first-night effects, and concluded that one night of recording does not represent a patient's

usual pattern of sleeping. Therefore, at least two nights of recordings are indicated, and only data from the second night of recordings are traditionally used. No differences in sleep across two consecutive nights of home PSG, however, were demonstrated in this group of MMT patients. Specifically, measures that reportedly showed first-night effects in other studies, such as REM latency, REM percent, Stage 1 percent, and SWS percent, were unchanged from night 1 to night 2 in this study. Unfamiliarity with a novel environment is one proposed origin of first-night effects for lab-based assessments. Thus, we may not have observed first-night effects because PSG took place in participants' homes. Alternatively, the sleep of these patients may have been sufficiently disrupted from other causes – including chronic methadone administration – that sensitivity to first-night effects could not be observed.

We acknowledge a caveat raised by evidence that prolonged adaptation to PSG may occur over several nights with variables showing stable values at different rates (15). Thus, one night for adaptation may be insufficient, and the sleep measures in our participants may have “normalized” with additional nights of recording. Kupfer and colleagues proposed that the absence of first-night effects is a marker of limited ability to adapt to novel environments (25), and Wauquier et al. question whether manifesting a first-night effect is a marker of a healthier clinical state or represents the central nervous system's adaptability to novel situations (12). Therefore, difficulty adapting to a novel sleep environment in only two days may play a role in sleep disturbance in opioid-dependent patients and paradoxically manifest as between-night stability in PSG results.

Participants in whom only one valid PSG was obtained had more disturbed sleep than MMT patients who completed two PSG nights. Moreover, this difference in sleep between groups with one vs. two nights of PSG could not be explained by demographics, subjective sleep disturbance (PSQI score), methadone dose, or illicit drug use. Possible explanations for greater abnormalities in the PSG of the single-night group include inherently worse sleep, greater susceptibility to sleep disturbance produced by the recording equipment, and more disrupted sleep environments.

This study has important implications for conducting home PSG in MMT patients. First, it is reasonable to assume that baseline sleep as measured by home PSG in this population remains relatively stable across two consecutive nights. Therefore, results from one night of recording can be considered sufficient for most study purposes. Second, excluding MMT patients who complete only one baseline night of PSG may unintentionally exclude patients with the most disturbed sleep, which is precisely the group that most warrants clinical investigation and attention. For research purposes, excluding this group could produce a skewed distribution of less disturbed sleep that might be mistaken as characterizing this population.

In conclusion, this is the first study to our knowledge that utilized home PSG in a sample of MMT patients, a potentially challenging group of patients to engage in complex research procedures. Given the high prevalence of sleep disturbance in MMT patients, further research in this area is indicated, especially because sleep disturbance has been linked to relapse in patients with other substance use disorders. Although standard sleep laboratory

protocols generally require two consecutive nights of PSG for allowing adaptation to a novel environment and recording procedures, such a requirement may place extra burden on research participants. Our finding of relatively stable sleep measures across two consecutive nights of study argues against this requirement. Even in situations, however, when investigators choose to adopt a standard two-night sleep protocol, loss of data can occur for numerous reasons (e.g., equipment failure or participants who are non-adherent to the study protocol). Under these circumstances, our results suggest that data obtained from a single night of recording can be used with reasonable confidence in its reliability.

Sleep complaints are pervasive in patients with opiate dependence enrolled in MMT. Further study is needed to determine whether poor sleep contributes to relapse in MMT patients and whether sleep problems in this population can be alleviated pharmacologically.

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Table 1

Sleep Parameters for Two Consecutive Nights in 36 MMT Patients.

	Night 1	Night 2
Sleep Parameter	Mean ($\pm$ SD)	Mean ($\pm$ SD)
Sleep Period Time (Minutes)	435 ($\pm$ 79)	433 ($\pm$ 95)
Total Sleep Time (Minutes)	370 ($\pm$ 79)	368 ($\pm$ 95)
Sleep Efficiency (%)	85.2 ($\pm$ 9.6)	84.7 ($\pm$ 11.0)
Wake after Sleep Onset (Minutes)	64 ($\pm$ 42)	66 ($\pm$ 45)
Stage 1 (Minutes)	8 ($\pm$ 6)	8 ($\pm$ 5)
Stage 2 (Minutes)	239 ($\pm$ 61)	239 ($\pm$ 68)
Slow Wave Sleep (Minutes)	56 ($\pm$ 28)	59 ($\pm$ 35)
REM (Minutes)	68 ($\pm$ 36)	63 ($\pm$ 38)
REM Latency (Minutes)	108 ($\pm$ 77)	96 ($\pm$ 71)
Stage 1 (%)	2.2 ($\pm$ 1.7)	2.1 ($\pm$ 1.4)
Stage 2 (%)	64.7 ($\pm$ 10.7)	65.6 ($\pm$ 11.6)
Slow Wave Sleep (%)	15.5 ($\pm$ 8.4)	16.1 ($\pm$ 10.0)
REM (%)	17.6 ($\pm$ 8.2)	16.1 ($\pm$ 8.2)
% Wake	14.7 ($\pm$ 9.6)	15.3 ($\pm$ 11.0)
Arousal Index	10.9 ($\pm$ 9.2)	11.8 ($\pm$ 13.8)

Table 2
Sleep Parameters by Night Completion Status

Sleep variables in participants who completed 2 PSG nights were averaged and group comparisons were made with participants who completed 1 PSG using t-tests and the nonparametric Wilcoxon rank-sum test.

	2 Nights (n = 36)	1 Night (n = 14)
Sleep Variable	Mean (± SD)	Mean (± SD)
Sleep Period Time (Minutes) (p < .05)	434 (± 78)	326 (± 116)
Total Sleep Time (Minutes) (p < .05)	369 (± 81)	271 (± 101)
Sleep Efficiency (%)	85.0 (± 9.6)	82.9 (± 9.5)
Wake after Sleep Onset (Minutes)	65 (± 40)	55 (± 36)
Stage 1 (Minutes)	8 (± 4)	6 (± 4)
Stage 2 (Minutes) (p < .05)	239 (± 58)	185 (± 68)
Slow Wave Sleep (Minutes)	57 (± 28)	43 (± 25)
REM (Minutes) (p < .05)	65 (± 33)	37 (± 20)
REM Latency (Minutes) (p < .05)	102 (± 54)	63 (± 47)
Stage 1 (%)	2.2 (± 1.3)	2.2 (± 1.0)
Stage 2 (%)	65.2 (± 10.0)	68.4 (± 9.4)
Slow Wave Sleep (%)	15.8 (± 8.0)	16.4 (± 8.1)
REM (%)	16.8 (± 7.2)	13.0 (± 5.8)
% Wake	15.2 (± 9.6)	17.1 (± 9.5)
Arousal Index	11.3 (± 11.2)	9.1 (± 11.5)