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Wireless Electroencephalography (EEG) to Monitor Sleep Among Patients Being Withdrawn from Opioids: Evidence of Feasibility and Utility

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Abstract

Sleep impairment is a common comorbid and debilitating symptom for persons with opioid use disorder (OUD). Research into underlying mechanisms and efficacious treatment interventions for OUD-related sleep problems requires both precise and physiologic measurements of sleep-related outcomes and impairment. This pilot examined the feasibility of a wireless sleep electroencephalography (EEG) monitor (Sleep Profiler™) to measure sleep outcomes and architecture among participants undergoing supervised opioid withdrawal. Sleep outcomes were compared to a self-reported sleep diary and opioid withdrawal ratings. Participants (n=8, 100% male) wore the wireless EEG 85.6% of scheduled nights. Wireless EEG detected measures of

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sleep architecture including changes in total, NREM and REM sleep time during study phases, whereas the diary detected changes in wakefulness only. Direct comparisons of five overlapping outcomes revealed lower sleep efficiency and sleep onset latency and higher awakenings and time spent awake from the wireless EEG versus sleep diary. Associations were evident between wireless EEG and increased withdrawal severity, lower sleep efficiency, less time in REM and non-REM stages 1 and 2, and more hydroxyzine treatment; sleep diary was associated with total sleep time and withdrawal only. Data provide initial evidence that a wireless EEG is a feasible and useful tool for objective monitoring of sleep in persons experiencing acute opioid withdrawal. Data are limited by the small and exclusively male sample, but provide a foundation for using wireless EEG sleep monitors for objective evaluation of sleep-related impairment in persons with OUD in support of mechanistic and treatment intervention research.

Keywords

opioid; withdrawal; sleep; EEG; buprenorphine

1. Introduction

Opioid use disorder (OUD) is a significant public health problem that produces substantial morbidity and mortality throughout the world. Persons with opioid physical dependence experience withdrawal upon opioid discontinuation that is characterized by intense physical discomfort, changes in mood, and sleep disturbance (Dunn, Huhn, Bergeria, Gipson, & Weerts, 2019). Sleep disturbance has emerged as an area of significant interest because it is a common, comorbid, and intractable feature of acute and protracted opioid (Dunn et al., 2019) and other drug withdrawal syndromes (Valentino & Volkow, 2020) that patients identify as a primary treatment goal (Furlow, 2016). Sleep disruption during opioid withdrawal has been associated with increased psychiatric severity (Burke et al., 2008; Dunn, Finan, Tompkins, & Strain, 2018; Gros, Milanak, Brady, & Back, 2013), continued opioid use (Barth et al., 2013; Burke et al., 2008), and poor treatment retention (Beswick et al., 2003).

The inter-relationship between opioid exposure and sleep disturbance is well established. Chronic opioid exposure impairs sleep in preclinical (Pacesovia, Novotný, & Bendová, 2016; Robert, Stinus, & Limoge, 1999; Young, Moreton, Meltzer, & Khazan, 1975) and human (Dunn et al., 2018; Kay, 1975) models, and the majority of persons entering treatment for OUD often report clinically-significant sleep impairment (Hartwell, Pfeifer, McCauley, Moran-Santa Maria, & Back, 2014; Nordmann et al., 2016; Peles, E., Schreiber, & Adelson, 2006; Peles, Einat, Schreiber, Hamburger, & Adelson, 2011; Stein et al., 2004). Yet few studies have evaluated the relationship between opioid withdrawal and sleep. One study found that better sleep was the only withdrawal item to differ between buprenorphine tapers deemed more or less efficacious (Dunn, Saulsgiver, Miller, Nuzzo, & Sigmon, 2015). Examination of electroencephalogram (EEG) using polysomnography (PSG) has found that heroin exposure decreases time in REM and that opioid withdrawal increases time spent in REM (Lewis, Oswald, Evans, Akindele, & Tompsett, 1970) in one study and decreases time spent in REM (19.2% vs. 25.5%) and REM episodes (1.6 vs. 4.2) compared to controls

in other studies (Howe, Hegge, & Phillips, 1980; Howe, Phillips, & Hegge, 1980; Howe, Phillips, & Hegge, 1981). PSG has also revealed that opioid withdrawal increases time spent awake (78.9% vs. 68.3%) and sleep onset latencies (216.8 vs. 80.9 minutes; Howe, Hegge, & Phillips, 1980) while decreasing slow wave sleep time relative to controls, respectively (Howe et al., 1980; Howe et al., 1980; Howe et al., 1981).

Though sleep continuity and architecture data can help elucidate mechanisms underlying opioid-related sleep disturbance and inform intervention strategies, several barriers to using conventional PSG during opioid withdrawal exist. PSG requires a trained technician, wired electrode placements across the scalp, face, and body, and a dedicated brick and mortar facility. Lab-based PSGs, which are normally considered moderately uncomfortable, are likely to be extremely uncomfortable during opioid withdrawal and make it challenging to collect sensitive sleep information during withdrawal. There have been no recent full-PSG examinations in patients being withdrawn from opioids.

This pilot study assessed the feasibility of a non-invasive, ambulatory, wireless 3-lead frontal EEG monitor (Sleep Profiler™) to assess sleep continuity and architecture in patients being withdrawn off opioids. The Sleep Profiler™ has strong PSG agreement in healthy subjects (Finan et al., 2016) and patients with insomnia and sleep apnea (Levendowski et al., 2017) but has not been evaluated in patients experiencing opioid withdrawal. This study assessed whether patients would wear and tolerate the device during an opioid taper, whether changes in sleep could be detected across taper phases, and how data from the wireless EEG compared to a self-reported sleep diary and opioid withdrawal ratings.

Methods

2.1 Participants:

Participants were recruited from a parent trial comparison of buprenorphine, tramadol-extended release (ER), and clonidine for opioid withdrawal (Dunn, Tompkins, Bigelow, & Strain, 2017). This study was approved by the Johns Hopkins University IRB as a subprotocol and eligible participants met parent study eligibility ((Dunn et al., 2017), which included physical dependence on opioids, and were excluded for scalp conditions that could interfere with EEG detection. All approached participants were eligible and agreed to participate and enrollment concluded (N=8) upon parent trial completion.

2.2 Parent Study Methods:

Participants were admitted to a residential unit for ≥28 days across three phases. During the stabilization phase all participants received morphine (30mg, SC) four times daily. During the taper phase participants were randomly-assigned to a double-blind, double-dummy, 7-day stepwise taper off morphine using buprenorphine, tramadol-ER, or clonidine. During the post-taper phase participants received double-blind, placebo-dosing. Hydroxyzine (50mg, PO) was available for sleep disturbance throughout the study. Participants earned $5 for completing the sleep diary each day; earnings were not contingent upon wireless EEG compliance.

2.3 Measures:

2.3.1 Sleep Profiler™: Wireless EEG was assessed using the Sleep Profiler™ (Advanced Brain Monitoring, Carlsbad, CA), which is affixed to the forehead with a flexible headband to collect EEG, electrooculogram (EOG), and electromyogram (EMG) readings. Single-use, gelled, snap-electrodes were attached to the device each night to record 3-channel frontal EEG, pulse rate, and head movements. The Sleep Profiler™ has a 16-hour battery life and is lightweight (2.5oz), making it a potentially feasible method for collecting sensitive sleep continuity and architecture data during opioid withdrawal. Participants were audibly guided through an impedance check by the Sleep Profiler™ each night and data were uploaded to an accompanying software program for sleep stage autoscoring. A board certified sleep specialist who was blinded to study phase also manually edited stages using a previously described process (Levendowski et al., 2017).

Participants were trained on the Sleep Profiler™ and provided assistance nightly as needed. They were instructed to wear the device on nine specific nights that corresponded to three consecutive nights each during the morphine, taper, and post-taper phases. This strategy aimed to balance data collection during three important periods while not influencing participant willingness to participate in the parent trial by requiring nightly use before Sleep Profiler™ tolerability under these circumstances was understood.

The following primary outcomes were collected from the Sleep Profiler™: total sleep time, sleep efficiency (time spent sleeping/time spent in bed; %), sleep onset latency, number of awakenings, time spent awake, wake after sleep onset (WASO), and percent of time and minutes spent in each sleep stage (non-REM stages 1, 2, 3, and REM). Additional outcomes (e.g., time spent snoring, nonsupine time, pulse during arousals, delta theta, alpha, sigma, and beta levels across sleep stages and waking) are not reported here. Compliance was defined as the percent of scheduled days the Sleep Profiler™ was worn by each participant.

2.3.2 Sleep Diary: Participants completed a daily consensus sleep diary (Carney et al., 2012) that yielded the following primary outcomes: total self-reported sleep time (duration of reported sleep between sleep onset and final awakening), sleep efficiency (time spent sleeping/time spent in bed; %), sleep onset latency, number of awakenings, WASO, and time spent awake.

2.3.3 Opioid Withdrawal: Participant withdrawal was assessed seven times daily using the Clinical Opiate Withdrawal Scale (COWS, range 0–48; Wesson & Ling, 2003), the Subjective Opiate Withdrawal Scale (SOWS, range 0–64; Handelsman et al., 1987), and a visual analog scale (VAS) for “Sick (range 0–100). Scores were summed, with higher values representing greater withdrawal severity, and primary outcomes were the peak scores on each day that sleep data were collected. Number of hydroxyzine doses on these days was also assessed.

2.4 Data Analysis

This study assessed the feasibility of using a wireless EEG to collect objective sleep continuity and architecture data from patients undergoing acute opioid withdrawal and

compared results to a conventional self-reported sleep diary. EEG compliance was evaluated as a measure of feasibility. The relative sensitivity of primary outcomes for detecting within-subject changes across study phases was assessed using repeated measures analyses of variance (ANOVAs), collapsing ratings together to evaluate main effects of study phase. Total sleep time, sleep efficiency, sleep onset latency, awakenings (#), and WASO were compared between the EEG and sleep diary as a function of phase (morphine, taper, post-taper) and measure (wireless EEG, sleep diary) using two-way repeated measures ANOVAs. Finally, relationships between sleep and withdrawal outcomes, independent of phase, were explored using Pearson two-way correlations. Given the exploratory nature of these analyses and the fact that missing data were largely attributed to participant attrition from the parent study, missing data were treated as missing and not interpolated. For all analyses, alpha was set at <0.05 and analyses were conducted using SPSS Inc. (version 25).

3. Results

3.1 Participants

Participants (n=8) were 100% male, 88% African American, a mean age of 46 (SD=6.5) years, and tapered using buprenorphine (25%), tramadol-ER (25%) and clonidine (50%). Seven (87.5%) study participants completed the parent study and one left during morphine stabilization. Withdrawal ratings for the COWS ($F(2,30)=11.95$, $p<.001$), SOWS ($F(2,30)=17.94$, $p<.001$), and VAS for “Sick” ($F(2,30)=16.59$, $p<.001$) varied significantly across phases, with withdrawal being highest during the taper, followed by morphine, and post-taper phases (Table 1).

3.2 Wireless EEG Compliance

Participants had good overall compliance (85.6%) with the wireless EEG. Compliance was highest during the morphine phase and lowest during the acute withdrawal period, when only 71.4% of participants wore the wireless EEG and for only 76% (16/21) scheduled nights. Compliance increased again during the post-taper phase, wherein 86% participants had complete compliance and the final participant had 66.6% compliance. Two participants also chose to wear the wireless EEG for more than 3 study nights during the morphine and taper periods, resulting in mean compliance rates of 133% and 166% for those periods, respectively (Figure 1).

3.3 Sleep Outcomes During Study Phases

Primary outcomes are reported in Table 1. Sleep efficiency exceeded 100% in 23% (14/61) of sleep diary ratings so were truncated to 100% for analyses. Repeated measures ANOVAs revealed different main effects of study phase depending upon the collection method. Wireless EEG yielded significantly higher total sleep time ($F(2,30)=6.19$, $p=0.006$) and time spent in REM sleep ($F(2,30)=7.09$, $p=.003$) during the post-taper relative to morphine and taper phases, whereas total sleep time rated by the sleep diary approached ($p=0.07$) but did not achieve significance. The sleep diary also yielded fewer reports of awakenings ($F(2,30)=4.69$, $p=0.017$) and time spent awake ($F(2,30)=6.55$, $p=0.004$) during the post-taper relative to other study phases, which was not observed by the wireless EEG.

Direct comparisons of overlapping outcomes suggested the wireless EEG and sleep diary identified different types of sleep disturbances (Figure 1). A significant main effect of phase ($F(2,30)=5.48$, $p=0.009$) was observed on total sleep time wherein more sleep occurred during the post-taper versus other phases, though no main effect of measure was observed. A significant main effect of phase ($F(2,30)=4.91$, $p=0.014$) and measure ($F(1,15)=16.17$, $p=0.001$) was observed for sleep efficiency, which was highest during the post-taper versus other phases and higher on the sleep diary than the wireless EEG. No main effect of phase was observed for sleep onset latency but a significant main effect of measure was observed ($F(1,15)=5.45$, $p=0.034$), whereby the sleep diary recorded longer sleep latencies than the wireless EEG. Number of awakenings did not reveal a main effect of phase but the main effect of measure was significant ($F(1,15)=90.02$, $p<.001$) and suggested the wireless EEG detected more awakenings than the sleep diary. Finally, there was no main effect of phase but a significant main effect of measure ($F(1,15)=67.89$, $p<.001$) on time spent awake, whereby the wireless EEG detected more time spent awake across phases than the sleep diary.

2.4 Correlations Between Outcomes

Several outcomes from the wireless EEG and the sleep diary were significantly correlated (Table 2). Wireless EEG-derived values for total sleep time, sleep efficiency, WASO, as well as some architecture outcomes, were positively associated with sleep diary outcomes. Despite large discrepancies in the number of awakenings detected by the wireless EEG and reported on the sleep diary, those two values were significantly correlated. Only the wireless EEG-derived values for time spent awake and number of cortical arousals had no significant associations.

Few sleep outcomes were correlated with withdrawal ratings (Table 2). COWS and SOWS total scores, and VAS ratings of “Sick”, were all significantly negatively associated with wireless EEG-derived percent of time spent in Non-REM sleep stages 1 and 2, and sleep diary ratings of time spent awake, with more severe withdrawal being associated with less sleep. VAS ratings of “Sick” were associated with wireless EEG -derived sleep efficiency and number of awakenings. Hydroxyzine use was also significantly associated with wireless EEG-derived time spent in REM sleep and sleep diary reports of time spent awake, as well as COWS, SOWS, and “Sick” ratings. The only variable from the sleep diary to be associated with withdrawal ratings was total sleep time.

4. Discussion

This study assessed the feasibility of a wireless EEG device (Sleep Profiler™) to collect objective information about sleep continuity and architecture from persons undergoing acute opioid withdrawal and compared results to a self-reported sleep diary. Outcomes suggest the wireless EEG was generally well-tolerated, as evidenced by good compliance, and provide preliminary evidence that both measures were sensitive to changes in sleep over time but that sleep impairment type and severity varied across collection methods.

Self-reported sleep diaries are routinely used in clinical and nonclinical populations (Carney et al., 2012), but are consistently discrepant from objective EEG/PSG results (Lauderdale,

Knutson, Yan, Liu, & Rathouz, 2008; O'Brien, Hart, & Wing, 2016), similar to what was observed here. This study also revealed unique strengths of the wireless EEG relative to the sleep diary; several sleep architecture outcomes available only from the wireless EEG were significantly associated with opioid withdrawal severity and wireless EEG protected against impossible results (e.g., sleep efficiency >100%). Direct comparison of measures also revealed that participants were over-estimating their sleep efficiency and sleep onset latency and under-estimating awakenings per night and time spent awake. This is consistent with prior research that found persons receiving methadone or buprenorphine for OUD consistently reported better sleep continuity on a sleep diary than what was observed with a wireless EEG (Finan et al., 2016). Although these differences could be due to the wireless EEG having a more precise definition of wakefulness that does not require conscious awareness of being awake, it is notable that awakenings and time spent awake were the only variables that differed across study phases for the sleep diary- introducing doubt to the validity of these self-reported outcomes.

The differences observed across detection measures could have clinical significance. Precise determination of sleep impairment is necessary to identify appropriate sleep intervention strategies (Bragazzi, Guglielmi, & Garbarino, 2019) and accurate understanding of sleep impairment could benefit non-OUD outcomes. For instance, the extended nighttime wakefulness observed here but underreported by participants has been previously associated with deleterious effects on mood (Baglioni et al., 2011), and may have consequences for persons with OUD as rates of clinically-significant mood disorders are higher within that population than the general public (Goldner, Lusted, Roerecke, Rehm, & Fischer, 2014). Sensitive measurement of sleep architecture could also be used to identify circadian disorders and sleep apneas across the opioid recovery continuum (Lydon-Staley et al., 2017). Apnea in particular is a major concern for persons with OUD; a large percentage of patients entering treatment for opioids present with central (≥60%) or obstructive (≥39%) sleep apnea (Hassamal, Miotto, Wang, & Saxon, 2016) and many additional patients develop apnea during treatment (Peles et al., 2011). Although studies have demonstrated the likelihood of apnea increases with more opioid exposures (Hassamal et al., 2016), the potential for apnea to resolve following opioid withdrawal remains unclear. Though the wireless EEG used here did not detect apneas, several other FDA-cleared wearable devices (e.g., WatchPat; Nox-T3), as well as a new version of the Sleep Profiler™, have been developed for apnea detection and should be included in future evaluations of sleep in persons with OUD.

This study was a pilot/feasibility study and results should be considered preliminary (Eacret, Veasey, & Blendy, 2020). It is likely that the good compliance observed with this 3-EEG lead device is partially due to its non-invasive nature and the decrease in compliance observed during the opioid taper is consistent with concerns that persons experiencing acute opioid withdrawal may not tolerate conventional PSG. Wireless EEG adds additional strengths for use during periods of acute opioid withdrawal, including that its application is less technical and time consuming than PSG, which reduces barriers for clinical use. Conversely, the wireless EEG does collect a leaner array of data than PSG that provides a less sensitive characterization than PSG. However, the extreme discomfort experienced by patients in acute withdrawal suggests even more minimally invasive sleep EEG technologies

(e.g., ear EEG; Zibrandtsen, Kidmose, Otto, Ibsen, & Kjaer, 2016) could be considered in future research.

Additional strengths of this study include the rigorous parent study design and enrollment of a predominantly Black participant sample, which supports efforts to understand social determinants of health and health disparities for both OUD and sleep-related outcomes (Eacret et al., 2020). The study is limited by the provision of hydroxyzine for sleep and the small and exclusively male sample, which obscures interpretation of results. Moreover, though this device has been validated against PSG in non-OUD samples, auto-staging may diverge from PSG during periods of poor sleep, supporting prospective validation of this device to PSG in persons with OUD. Related to this is the potential for some awakenings to have been apneas. Finally, specific reasons for noncompliance that could have informed future studies were not collected.

Overall, these data suggest a wireless EEG was a feasible and sensitive method for detecting differences in sleep before, during, and after acute opioid withdrawal. Direct comparison of the wireless EEG and sleep diary revealed the type and severity of sleep impairment varied depending upon the measures, with the wireless EEG identifying more severe problems than participants reported. Ultimately, this study supports additional examination of a wireless sleep EEG monitor for measuring sleep-related outcomes in OUD research studies.

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Public Health Significance:

Many people who are withdrawing off of opioids experience severe and clinically-significant levels of sleep impairment and insomnia. In order to learn more about sleep impairment and appropriate treatment strategies, we must identify comfortable and precise ways to measure sleep in patients experiencing withdrawal. This study provides initial evidence that a commercially-available, wireless, ambulatory EEG sleep monitor was accepted by patients and provided information that was more closely associated to measures of withdrawal than a standard sleep diary.

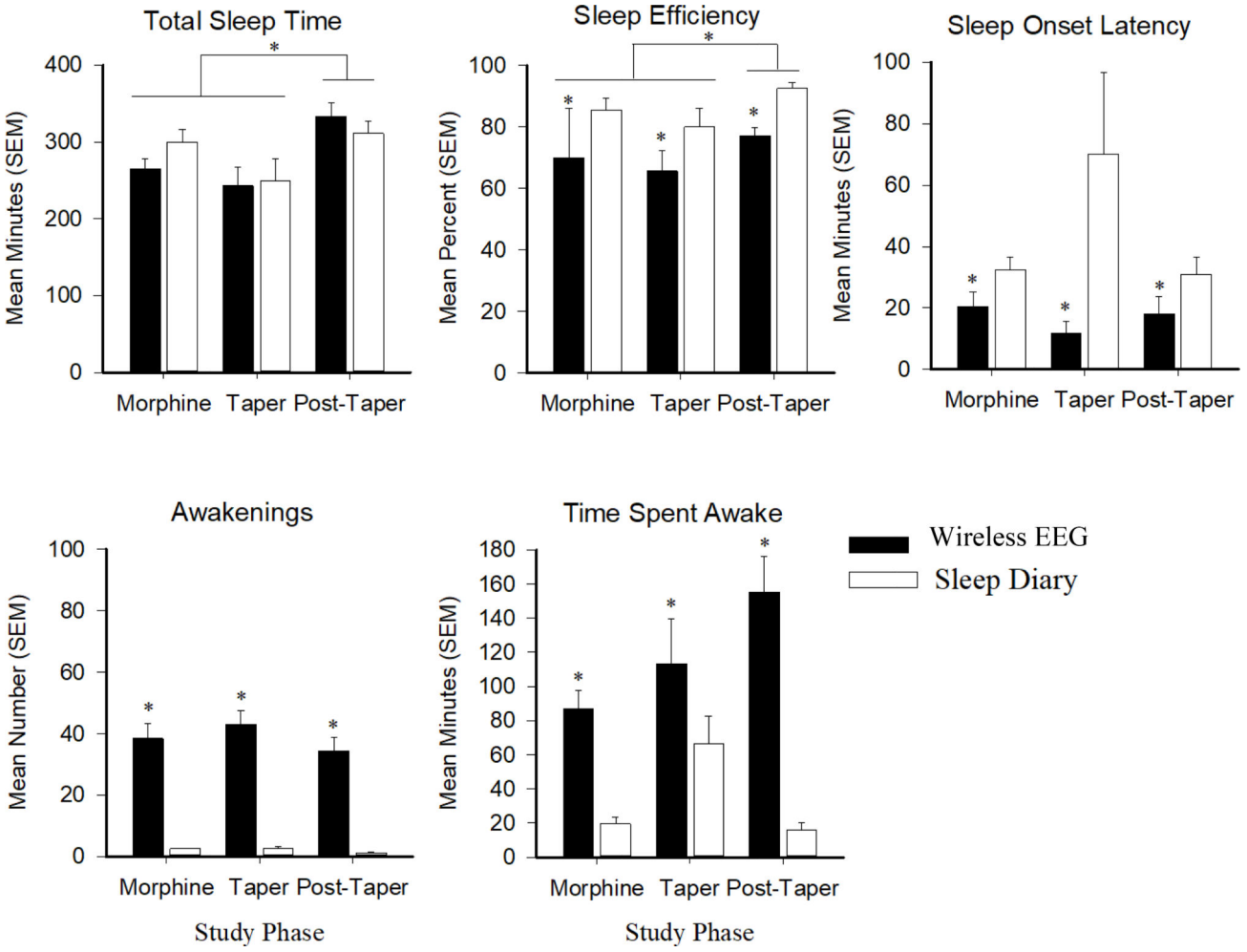

Figure 1. Sleep Outcomes

Graphs represent five outcomes that overlapped between the wireless EEG (Sleep Profiler™) and sleep diary. Data present results collected from the wireless EEG (Sleep Profiler™; filled bars) and self-reported sleep diary (open bars) as a function of the study phase (morphine stabilization, taper, and post-taper phase) across the X-axis. Data all represent mean (SEM) outcomes. Asterisks signify significant main effects of measure when placed over individual bars and significant main effects of time are signified by the lines and asterisks. Alpha is set at 0.05.

Table 1.

Sleep and Withdrawal Outcomes

	Morphine Stabilization N=8	Taper N=5	Post-Taper N=7	p-value[a]
Sleep Profiler				
Sleep Outcomes				
Total Sleep Time (min)	265.9 (67.0)[a]	243.01 (101.7)[a]	333.3 (76.1)b	<.01
Sleep Efficiency (%)	70.1 (16.1)	65.7 (27.1)	77.2 (12.0)	0.07
Sleep Onset Latency (min)	20.6 (23.1)	11.9 (15.5)	18.2 (24.6)	0.59
Wake After Sleep Onset (min)	100.1 (73.2)	120.1 (116.8)	81.1 (54.1)	0.18
Time Spent Awake				
Awakenings (number)	38.4 (25.2)	43.1 (18.2)	34.4 (20.3)	0.60
Time Spent Awake (min)	86.9 (54.0)	113.3 (1.04.1)	155.2 (94.6)	0.16
Corticol Arousals (number)	103.8 (103.5)	72.9 (65.1)	95.8 (54.2)	0.50
Sleep Architecture				
Rapid Eye Movement (REM)				
Percent	21.7(9.6)	22.9 (13.6)	29.2 (12.4)	0.12
Time (min)	58.5 (33.4)[a]	55.0 (42.8)[a]	100.2 (59.1)b	0.03
Non-REM Stage 1				
Percent	22.3 (13.6)	28.4 (13.7)	16.7 (8.1)	0.12
Time (min)	55.7 (32.5)	63.8 (31.9)	53.7 (22.9)	0.58
Non-REM Stage 2				
Percent	49.6 (11.3)	43.6 (17.1)	47.2 (13.9)	0.54
Time (min)	134.1 (53.4)	110.5 (57.2)	151.9 (42.0)	0.26
Non-REM Stage 3				
Percent	6.4 (5.8)	5.0 (7.0)	6.8 (15.6)	0.69
Time (min)	16.3 (13.0)	13.8 (19.7)	27.5 (72.1)	0.50
Sleep Diary				
Total Sleep Time (min)	299.7 (84.8)	249.9 (118.4)	311.15 (70.1)	0.07
Sleep Efficiency (%)	85.4(3.9)	80.0(6.2)	92.7 (1.7)	0.08
Sleep Onset Latency (min)	32.4 (21.0)	70.0 (105.9)	31.0 (25.3)	0.10
Awakenings (number)	2.5 (1.2)[a]	2.8 (1.6)[a]	1.3 (,1.2)b	0.02
Time Spent Awake (min)	24.9 (19.5)[a]	66.5 (65.2)b	16.1 (17.2)[a]	0.04
Withdrawal Outcomes				
COWS (total score, 0–48)	5.4 (7.4)[a]	12.1 (10.8)b	2.0 (3.3)[a]	<.001
SOWS (total score, 0–64)	2.4 (2.1)[a]	4.8 (2.4)b	3.3 (1.8)c	<.001
VAS “Sick” (0–100)	6.7 (15.0)[a]	48.4 (29.9)b	9.7 (12.0)[a]	<.001
Hydroxyzine (number taken)	0.3 (0.5)	1 1(16)	0.5 (0.6)	0.07

Data based upon observations collected from participants during morphine stabilization (n=25), taper (n=16), and post-taper (n=20) periods. Data represent means (standard deviation); letters signify non-corrected significant differences between phases. Participants contributed >1 observation

per phase. min=minutes; REM=rapid eye movement; COWS=Clinical Opiate Withdrawal Scale; SOWS=Subjective Opiate Withdrawal Scale; Visual Analog Scale

[a.] When Bonferroni conections for multiple comparisons were applied, only Sleep Profiler, Total Sleep Time and withdrawal rating scales (COWS, SOWS, VAS) remained significant.

Table 2.

Correlations Between Wireless EEG, Sleep Diary, Withdrawal Ratings

	Self-reported Measures								
	Total Sleep Time	**Sleep Efficiency**	**Sleep Onset Latency**	**Awakenings (#)**	**Time Spent Awake**	**COWS Score**	**SOWS Score**	**VAS "Sick" (0–100)**	**Hydroxyzine (#)**
Wireless EEG-derived Outcomes									
Total Sleep Time	.518**	.284*	−.405**	−.363**	−0.081	−0.17	−0.061	−0.24	0.071
Sleep Efficiency	.471**	.291*	−.499**	−.280*	−0.006	−0.024	−0.096	−.271*	0.145
Sleep Onset Tatency	0.094	−0.05	−0.189	−0.151	−0.249	−0.148	−0.036	−0.092	−0.231
WASO	−.376**	0.007	.584**	.326*	0.097	0.005	0.112	0.252	−0.05
Awakenings	−0.128	0.029	0.152	.268*	0.145	−0.043	0.067	.283*	−0.103
Time Spent Awake	−0.018	−0.086	0.201	0.06	−0.107	−0.055	0.03	0.173	−0.124
Corticol Arousals	0.02	0.086	−0.066	−0.139	−0.12	−0.042	−0.174	−0.026	−0.123
REM, percent	.261*	0.184	−0.042	−0.061	0.018	−0.045	0.043	0.019	.267*
REM, time	.501**	.265*	−0.227	−.268*	−0.064	−0.167	−0.065	−0.112	0.208
NREM1, percent	−0.22	−0.063	0.043	0.207	0.124	.342**	.263*	.420**	0.061
NREM1, time	0.101	0.123	−0.208	0.049	0.121	0.194	0.194	.262*	0.084
NREM2, percent	0.115	−0.066	0.046	−0.232	−0.148	−.317*	−.317*	−0.244	−0.226
NREM2, time	.472**	0.136	−.275*	−.398**	−0.143	−.308*	−.256*	−.302*	−0.113
NREM3, percent	−0.192	−0.047	−0.064	0.123	0.024	0.058	0.054	−0.22	−0.08
NREM3, time	−0.159	0.022	−0.075	0.02	0.001	0.085	0.124	−0.16	−0.01

Wireless EEG used was the Sleep Profiler. WASO=wake after sleep onset; REM=rapid eye movement; NREM=non-rapid eye movement; COWS=Clinical Opiate Withdrawal Scale; SOWS=Subjective Opiate Wilhdrawal Scale; VAS=Visual Analog Scale

Two-tailed Pearson correlations

** Correlation is significant at the 0.01 level

* Correlation is significant at the 0.05 level.