Seizure: European Journal of Epilepsy 65 (2019) 124–128

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Sleep disturbances in patients with psychogenic non-epileptic seizures: Is it all subjective? A prospective pilot study of sleep-wake patterns

Véronique Latreille[a], Barbara A. Dworetzky[a], Gaston Baslet[b], Milena Pavlova[a,*]

[a] Brigham and Women's Hospital, Department of Neurology, Harvard Medical School, Boston, MA, USA
[b] Brigham and Women's Hospital, Department of Psychiatry, Harvard Medical School, Boston, MA, USA

ARTICLE INFO

Keywords:
Psychogenic non-epileptic seizures
Epilepsy
Sleep
Electroencephalography
Actigraphy

ABSTRACT

Purpose: Patients with psychogenic non-epileptic seizures (PNES) frequently complain of poor sleep, yet there are few and inconsistent data supporting objective sleep disturbances in this population. In this prospective observational study, we aimed to compare objective and subjective sleep-wake patterns in patients with PNES with those with epilepsy.

Methods: Subjects were recruited through the Brigham and Women's Epilepsy Monitoring Unit (EMU) over a 6-month period, and were diagnosed as having PNES or epilepsy by experts using video-electroencephalography (v-EEG). Sleep-wake patterns were objectively examined using EEG and actigraphy during EMU admission. Subjects also completed several validated questionnaires on sleep.

Results: Twenty-seven subjects, including 17 with PNES and 10 with epilepsy were enrolled in the study. Compared to controls with epilepsy, PNES subjects showed greater sleep onset latency (48.7 ± 47.5 min vs 14.0 ± 13.4 min; $p = 0.02$). Otherwise, sleep architecture was similar between the groups. However, subjectively, PNES subjects reported worse sleep quality (10.8 ± 5.1 vs 5.8 ± 2.9; $p = 0.01$) and were more likely to meet clinical criteria for insomnia relative to epilepsy subjects (50% vs 10%, $p = 0.05$). Moreover, a higher proportion of PNES subjects reported taking medications for sleep (44% vs 0%, $p = 0.01$).

Conclusion: Overall, we found more evidence for a subjective basis rather than a pathophysiological nature for the reported sleep disturbances in PNES subjects. In addition to educating PNES patients on the importance of maintaining good sleep habits, clinicians should address sleep complaints and screen for insomnia, as effective treatments are available and may improve overall health.

1. Introduction

Poor sleep is a frequent complaint of patients with psychogenic non-epileptic seizures (PNES). Our group has recently reported that PNES subjects more frequently complained of poor sleep patterns relative to those with epilepsy [1], however the study was limited by use of a single item from the Beck Depression Inventory to assess changes in sleep patterns. Currently, little is known about the pattern and cause of sleep problems in PNES. One prior study investigated sleep architecture of 8 PNES and 10 epilepsy subjects using EEG recordings in the Epilepsy Monitoring Unit (EMU) [2]. Results showed a slightly greater proportion of rapid-eye-movement (REM) sleep in PNES relative to epilepsy subjects, while all the other sleep parameters remained similar across the groups. According to the authors, this higher REM sleep proportion may be related to comorbid depression in PNES patients, as individuals with major depression tend to show increased REM sleep [2]. More recently, Popkirov et al. (2018) investigated the prevalence of sleep disorders in a cohort of 22 patients with PNES and 44 with epilepsy undergoing an evaluation in the EMU. They found a similar proportion of sleep-disordered breathing across the groups, while periodic limb movement disorder was more frequent in PNES patients relative to those with epilepsy [3]. By contrast to Bazil et al's findings, no group difference in REM sleep duration was observed; rather, patients with PNES showed less slow-wave sleep, as compared to those with epilepsy.

Taken together, these studies suggest that sleep complaints are frequent in patients with PNES, but there is inconsistent objective evidence of disrupted sleep architecture in this group as compared to patients with epilepsy. Moreover, it may be that in PNES patients, the nature of sleep disturbances may represent a greater tendency towards somatization, an extension of the existing conversion symptoms that are associated with PNES, as about 70% of these individuals have other comorbid functional disorders [4]. In this prospective observational

* Corresponding author at: Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA.
E-mail address: mpavlova@bwh.harvard.edu (M. Pavlova).

https://doi.org/10.1016/j.seizure.2019.01.016
Received 16 November 2018; Received in revised form 14 January 2019; Accepted 17 January 2019

study, we aimed to examine subjective (validated sleep questionnaires) and objective (EEG, actigraphy) sleep-wake patterns in adult PNES and epilepsy patients undergoing long-term video-EEG monitoring.

2. Materials and methods

2.1. Participants

Subjects were adults referred over a 6-month period between 2/7/2018 and 8/6/2018 to the EMU at Brigham and Women's Hospital for diagnosis clarification or pre-surgical evaluation. PNES was diagnosed by experts and based on current clinical criteria [4]. Patients were categorized as (i) documented PNES if a typical episode was captured on video-EEG; and (ii) probable PNES if no typical episode was captured on video-EEG, but PNES suspicion is high based on clinical history, EEG, and event semiology. Epilepsy was diagnosed by board certified epileptologists based on history, semiology, and EEG findings. Subjects diagnosed with both epilepsy and PNES were excluded from the analyses. This study was approved by the institutional review board. All subjects gave written informed consent.

2.2. Objective sleep measures

All patients underwent standard video-EEG monitoring. The EEG montage included 19 scalp electrodes (International 10–20 system; Fp1, Fp2, F3, F4, Fz, F7, F8, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1, and O2) and electrocardiographic recordings. Sleep was visually scored by a technologist blinded to patient diagnosis on 30-s epochs according to current criteria [5]. We included for analysis the second or third night of recording following EMU admission to control for potential first-night effects (lighter than habitual sleep related to the new environment). However, in three patients who were discharged from the hospital one day following enrollment in the study, the first night of recording was used. Nights of "prescribed" sleep restriction were excluded from the analyses. As part of the standard EMU protocol, during the sleep study, antiepileptic drugs (AEDs) were tapered down but not completely withdrawn (except for patients with high suspicion of PNES). Subjects slept at their preferred times during the night. To assess sleep onset latency, we determined the time at "lights OFF" in the evening based on light data from the actigraphy sensor (see below) combined with sleep diaries (time at which subjects prepared to sleep and turned off the lights). The end of EEG recording was set around 6:30am per internal clinical routine procedures (typical time for vital signs measurements, breakfast, etc.). Sleep architecture variables included total sleep time, sleep latency and efficiency, REM sleep latency, time spent awake after sleep onset, sleep stages duration, and EEG arousal index (number per hour of sleep).

In addition to video-EEG, sleep-wake patterns were monitored using a wrist-worn actigraphy sensor (Actiwatch Spectrum Plus, Phillips Respironics, USA). Actigraphy objectively measures sleep parameters and motor activity using an accelerometer. The device is also equipped with a light sensor to provide photopic illuminance. Subjects wore the actigraphy device throughout the study period in the EMU. Actigraphy-based sleep variables included total sleep time, sleep latency and efficiency, time spent awake after sleep onset, and number of awakenings. As a measure of daytime and nighttime rest-activity, we also computed the ratio of activity counts during the day (7am to 9:59pm) and the night periods (10 pm to 6:59am) divided on the total 24-hr activity counts.

2.3. Subjective sleep measures

At the beginning of their EMU admission, all participants were asked to complete five validated sleep questionnaires. (*1*) The Pittsburgh Sleep Quality Index (PSQI) consists of a 19-item questionnaire assessing sleep quality over the last month. We included for analysis the PSQI total score (higher score indicating worse sleep quality), averaged reported total sleep time, sleep onset latency, sleep efficiency (time spent asleep/time spent in bed * 100), overall sleep quality, use of drugs for sleep, and number of patients with scores ≥ 7 (clinically impaired sleep quality). (*2*) The Insomnia Severity Index (ISI) consists of 7 items assessing the severity of insomnia symptoms over the last 2 weeks. Clinically, a score ≥ 15 indicates moderate to severe insomnia. We also examined the impact (moderate to severe) of insomnia symptoms on daily function impairment (item 7). (*3*) The Epworth Sleepiness Scale (ESS) measures daytime somnolence, with a score ≥ 10 indicating excessive daytime sleepiness. (*4*) The Morningness-Eveningness Questionnaire (MEQ) consists of 19 questions to assess chronotype on a morning-evening dimension: lower scores reflect a tendency for morningness, while higher scores reflect eveningness. (*5*) The Nightmare Distress Questionnaire (NDQ) is a 13-item tool to measure nightmare distress and its effects on well-being and daily function (higher scores indicate higher distress). Subjects also completed a daily sleep diary during EMU admission.

2.4. Comorbid psychiatric and sleep disorders

Diagnoses of psychiatric disorders were established either by (*1*) an extensive semi-structured psychiatric interview with an expert neuropsychiatrist (GB) for all patients with PNES and the majority of epilepsy patients (about 60%), or (*2*) routine clinical screening with the physician. Diagnoses of comorbid sleep disorders were based on clinical chart review, and thus established before EMU admission.

2.5. Statistical analysis

Sleep comparisons between patients with PNES and those with epilepsy were performed using independent sample *t*-test or non-parametric Mann-Whitney U test for continuous data, and Pearson's chi-square test for categorical data. Pearson correlation was used to assess the relationships between objective and subjective sleep measures. Significance was set at $p < 0.05$.

3. Results

Forty-one subjects undergoing video-EEG monitoring at Brigham and Women's Hospital were approached for participation in the study between 2/7/2018 and 8/6/2018. Ten subjects (2 with suspected PNES and 8 with epilepsy) declined to participate. Thirty-one subjects were recruited in the study. Three subjects had indeterminate video-EEG studies (possible physiologic non-epileptic seizures) and were excluded from analysis. One subject was excluded because of mixed epilepsy and documented PNES. Consequently, 27 total subjects, 17 patients with PNES (11 documented and 6 probable) and 10 with epilepsy, were included in the study analysis.

Demographic and clinical characteristics of all PNES and epilepsy subjects are presented in Table 1. We combined both documented and probable PNES subjects into one group given the small number of subjects in each category of diagnostic certainty, and because they did not differ on any clinical variables. On average, subjects were enrolled in the study for 4.0 ± 2.9 days (PNES, 3.5 ± 2.3 days; Epilepsy, 4.9 ± 3.7 days). All epilepsy subjects had medically refractory focal seizures (8 left temporal, 1 right parietal, and 1 bitemporal). Based on clinical history, two epilepsy subjects had occasional seizures during sleep. In the PNES group, two subjects reported having events during sleep, but these were not observed during EMU admission. As expected, antidepressant use was more common in subjects with PNES than epilepsy. Sleep disorders were diagnosed (prior to EMU admission) in almost half of the PNES patients (8/17), with obstructive sleep apnea the most common diagnosis (4/8). As expected, comorbid psychiatric disorders were more frequent in PNES subjects relative to those with epilepsy, particularly anxiety and post-traumatic stress disorder.

Table 1
Demographic and clinical data of all PNES and epilepsy patients.

	PNES n = 17	Epilepsy n = 10	*p*
Age, years	40.5 ± 14.3	47.7 ± 13.4	0.21
Sex, m/f	4/13	4/6	0.37
Education, years	12.9 ± 2.6	13.0 ± 2.2	0.95
Duration of disease, years*	11.3 ± 16.7	20.0 ± 17.0	0.21
Non-epileptic/seizure frequency, per month			0.48
n with < 1	4	4	
n with 1-2	7	2	
n with > 3	6	4	
Number of events during admission			0.14
n with 0	8	1	
n with 1-2	7	7	
n with > 3	2	2	
Number of AEDs at admission			0.14
n with 0	5	0	
n with 1-2	12	9	
n with > 3	0	1	
Benzodiazepine use, n (%)	5 (29)	1 (10)	0.24
Antidepressant use, n (%)	12 (71)	2 (20)	**0.01**
Sedative-hypnotic use, n (%)	1 (6)	0 (0)	0.44
Prior comorbid sleep disorders, n (%)	8 (47)	3 (30)	0.38
Insomnia	1	0	
Obstructive sleep apnea	4	3	
Restless leg syndrome	2	0	
Periodic limb movement of sleep	1	0	
Comorbid psychiatric disorders, n (%)	16 (94)	6 (60)	**0.03**
Mood disorder	6	3	
Anxiety disorder	9	2	
Post-traumatic stress disorder	10	1	
Psychotic disorder	0	1	

* Mann-Whitney U test. AED = Antiepileptic drug. Results are expressed as mean ± standard deviation, unless otherwise noted.

3.1. Objective sleep

EEG data from one epilepsy subject was not usable because of technical issues with the sleep EEG recording. We also excluded from the analysis two more subjects (documented PNES) because they were sleep deprived during the study period (second and third nights). Thus, EEG-based sleep architecture data from 24 patients (15 with PNES and 9 with epilepsy) were analyzed. Results are presented in Table 2.

Based on EEG scoring, subjects with PNES showed increased sleep onset latency as compared to those with epilepsy. We also found a trend towards reduced REM sleep in PNES relative to epilepsy. Otherwise, sleep architecture was similar between groups. Similarly, we found no significant difference between the groups for any actigraphy-based sleep measures (including sleep latency, by contrast to sleep EEG results).

Table 2
Objective sleep data of all subjects.

EEG sleep architecture	PNES	Epilepsy	*p*
Total sleep time, min	379.7 ± 97.5	337.8 ± 62.0	0.29
Sleep latency, min*	48.7 ± 47.5	14.0 ± 13.4	**0.02**
REM latency, min	170.6 ± 81.3	109.9 ± 124.0	0.18
Sleep efficiency, %*	75.8 ± 5.4	79.8 ± 16.7	0.20
Stage N1 %	5.2 ± 3.2	3.5 ± 1.6	0.16
Stage N2 %	54.5 ± 10.5	49.8 ± 8.7	0.29
Stage N3 %	22.8 ± 9.8	24.0 ± 7.6	0.78
Stage REM %	16.6 ± 8.6	22.8 ± 6.5	0.09
Wake after sleep onset, min*	69.4 ± 67.5	80.0 ± 100.9	0.95
EEG arousals index*	9.8 ± 5.6	8.7 ± 3.4	0.85
Actigraphy-based sleep			
Total sleep time, min	483.5 ± 95.6	426.5 ± 44.9	0.11
Sleep latency, min*	18.1 ± 20.7	19.0 ± 25.4	0.91
Sleep efficiency, %*	85.2 ± 10.1	85.8 ± 6.5	0.74
Wake after sleep onset, min*	55.2 ± 53.9	49.8 ± 34.8	0.70
Number of awakenings*	49.7 ± 24.7	40.8 ± 22.9	0.39
Daytime activity ratio, %	75.4 ± 14.2	79.0 ± 9.8	0.51
Nighttime activity ratio, %	24.6 ± 14.2	21.0 ± 9.8	0.51

* Mann-Whitney U test. REM: Rapid-eye-movement. Results are expressed as mean ± standard deviation.

Table 3
Subjective sleep data of all subjects.

	PNES	Epilepsy	*P*
PSQI, total score	10.8 ± 5.1	5.8 ± 2.9	**0.01**
PSQI ≥ 7, n (%)	13 (81)	4 (40)	**0.03**
Mean bed time	22:58 ± 2:11	22:09 ± 0:54	0.28
Mean wake time	7:28 ± 2:12	7:07 ± 1:47	0.75
Mean total sleep time, hrs	6.1 ± 2.0	7.3 ± 1.2	0.11
Mean sleep latency, min*	82.5 ± 112.4	22.8 ± 13.9	0.17
Mean sleep efficiency, %	74.2 ± 20.3	82.2 ± 11.8	0.27
Sleep quality: Fairly bad to very bad	11 (69)	1 (10)	**0.003**
Sleep drugs use, n (%)	7 (44)	0 (0)	**0.01**
ISI, total score	14.3 ± 8.2	10.3 ± 5.6	0.21
ISI ≥ 15, n (%)	8 (50)	1 (10)	0.05
Impaired daytime function, n (%)	11 (65)	4 (40)	0.21
ESS, total score	8.9 ± 4.5	8.2 ± 4.8	0.71
ESS ≥ 10, n (%)	8 (50)	4 (40)	0.79
MEQ, total score	51.8 ± 14.9	59.1 ± 9.6	0.13
NDQ, total score	13.9 ± 11.4	7.4 ± 6.1	0.18

* Mann-Whitney *U* test. PSQI: Pittsburgh Sleep Quality Index; ISI: Insomnia Severity Index; ESS: Epworth Sleepiness Scale; MEQ: Morningness-Eveningness Questionnaire; NDQ: Nightmare Distress Questionnaire. Impaired daytime function is based on item 7 of the ISI. Results are expressed as mean ± standard deviation, unless otherwise noted.

3.2. Subjective sleep

Subjective sleep data are presented in Table 3. Of note, two subjects (1 with documented PNES and 1 with epilepsy) did not complete the sleep questionnaires, and therefore data was available for 16 PNES and 9 epilepsy patients. Compared to those with epilepsy, PNES subjects reported significantly worse sleep quality as measured by the total PSQI score. A higher proportion of PNES subjects also reported sleeping very poorly, and needed to take medications for sleep (while none in the epilepsy group took sleep medications). Although the differences did not reach statistical significance due to lack of power and high variability, PNES subjects reported sleeping less on average and took longer to fall asleep than controls with epilepsy. Almost half of the PNES subjects reported taking more than one hour to fall asleep, and 4 out of 16 reported taking 2-3 h to sleep, which was not the case in any epilepsy subjects. A marginally significant difference was found for insomnia, with a higher proportion of PNES subjects reporting insomnia symptoms meeting clinical criteria for moderate to severe insomnia (ISI ≥ 15) relative to those with epilepsy. Although the difference did not reach statistical significance, PNES subjects tended to report more distress symptoms related to their nightmares relative to those with epilepsy. Daytime sleepiness and chronotype were similar between the groups.

We performed exploratory correlations to determine whether worse sleep problems (PSQI and ISI total scores) were associated with greater EEG sleep latency in all subjects, but found no significant relationship ($r < 0.15$, $p > 0.05$). Given the well-known relationships between psychiatric symptoms and poor sleep quality, we aimed to explore whether worse depressive and somatic symptoms and poorer quality of life were associated with reduced sleep quality (both objective and subjective). To do so, we retrieved scores from three questionnaires: (*1*) the Beck Depression Inventory, 2nd Ed. for severity of depressive symptoms; (*2*) the Patient Health Questionnaire-15 for severity of somatic symptoms, and (*3*) the Quality of Life in Epilepsy Inventory, 10-item for overall quality of life. These scales were completed in a subset of 10 subjects with PNES as part of an independent study protocol on mental health management in PNES. In this small subset of PNES

subjects, Pearson correlation revealed significant positive associations between overall quality of life and sleep latency as measured by EEG ($r = 0.78$, $p = 0.02$), as well as between severity of somatic symptoms and subjective sleep quality using the PSQI ($r = 0.71$, $p = 0.03$), indicating that greater sleep latency is associated with poorer quality of life, and worse somatic symptoms are linked to poorer perceived sleep quality.

4. Discussion

Our pilot study revealed that poor quality sleep is more commonly reported as a problem in patients with PNES compared to those with epilepsy. Indeed, PNES subjects more frequently complain of overall poor sleep quality, and a high proportion – almost 70% – report having fairly bad to very bad sleep. In addition, they are also more likely to take medications for sleep, while this was not observed in any of the epilepsy patients. A greater proportion of PNES subjects met clinical criteria for moderate to severe insomnia. Interestingly, only one subject with PNES was diagnosed with insomnia prior to EMU admission, whereas half of the group reported clinically significant insomnia symptoms during the study. This may reflect that during clinical routine visits, time constraint limits the focus of the discussion to the seizures and other major health issues, and thus sleep may be only superficially discussed. Methodological issues related to the inconsistency of documentation across providers through the electronic record system can also explain this discrepancy. Finally, it is possible that subjects with PNES were more sensitive to the hospital setting given their psychological vulnerability, which might have exacerbated the rating of their insomnia symptoms during our study. However, when completing the questionnaires at the beginning of the admission, all participants were specifically asked to rate their sleep quality over the past two weeks. Therefore, it is less likely that these insomnia symptoms were all situational or related to the hospital admission.

Objectively scored sleep EEG also indicated that PNES subjects on average took more time to fall asleep. This was not confirmed by actigraphy; both groups had similar actigraphy-based sleep latency values, and showed similar motor activity during nighttime as well as daytime. However, as the sensor measures movement, it may be underestimating sleep latency when subjects are staying still, though awake. Otherwise, sleep architecture was largely similar between PNES and epilepsy subjects. Overall, in this pilot observational study, we found more evidence for a subjective/functional basis rather than a pathophysiological nature for the reported sleep disturbances in PNES patients. This is in line with a prior study using actigraphy in patients with functional tremor that found a greater mismatch between the subjective and objective estimation of tremor level in patients with psychogenic tremor relative to those with organic tremor [6].

Our results are also consistent with our prior retrospective study showing that PNES subjects more frequently complained of poor sleep patterns relative to those with epilepsy [1], as well as prior reports showing poorer sleep quality in subjects with PNES using the PSQI [7]. Similarly, in a large sample of subjects with possible functional neurological disorders, including PNES, a recent study found that 89% of patients were at high risk of having a clinically-significant insomnia [8]. They also reported worse sleep quality, reduced total sleep time and sleep efficiency as compared to a normative sample, and these were negatively associated with functional impairment in daily living [8]. Regarding objective sleep architecture, although the difference did not reach statistical significance, we found a slightly lower proportion of REM sleep in PNES subjects as compared to those with epilepsy. This contrasts with the findings from Bazil's group (2003) who found greater REM sleep percentages in PNES patients. This difference may be due to the fact that antidepressant medications were stopped in Bazil's study, which was not the case in our subjects, and thus this increased REM sleep proportion in PNES subjects may represent a REM rebound. Nevertheless, similar to the recent study of Popkirov et al. (2018), we found that sleep architecture was overall comparable between PNES and epilepsy subjects.

Taken altogether, we found limited objective evidence supporting the sleep complaints in the PNES group. Although PNES subjects showed greater sleep latency on sleep EEG, it was not linked to subjective reports of poor sleep quality or insomnia symptoms. However, in a subset of our PNES cohort, greater EEG sleep latency was associated with poorer quality of life, and interestingly, poorer perceived sleep quality was associated with worse somatic symptomatology. Altogether, our main results and these exploratory findings suggest that the nature of the reported sleep problems may be more somatic than physiologic in PNES subjects.

Importantly, notwithstanding the nature of the sleep problems, these are usually easily managed with adequate interventions and thus treatment should be offered to any patient reporting sleep disturbances. Caution should be taken however when prescribing sleep medications, as PNES patients already take a lot of drugs for various medical comorbidities, and these could have a negative impact on daytime functioning (decreased energy, worse memory), without actually relieving their complaints of poor sleep. Other therapies aimed at treating somatic symptoms disorders or insomnia should be considered first. Particularly, cognitive behavioral therapies (CBT) and mindfulness-based approaches have been found to be effective in reducing PNES events and improving health outcomes [9]. CBT for insomnia is also the first choice of treatment for chronic insomnia symptoms and mindfulness-based interventions have shown positive results as well [10]. In addition to educating patients on the importance of maintaining good sleep hygiene, CBT and mindfulness approaches can help modify the patient's negative thoughts and disbeliefs about sleep, thereby improving daytime function and quality of life. This is particularly relevant as the nature of sleep complaints in PNES, based on this study, seems primarily driven by somatic focus, a target of CBT and mindfulness-based approaches.

Some limitations of our study should be mentioned. It is a pilot study performed in a small sample of patients with PNES and epilepsy while they were monitored in the EMU. We acknowledge that the EMU is not the ideal setting to study sleep-wake patterns, as patients are monitored continuously for several days in a novel environment which is not always sleep-friendly at night (noises, lights, tests), and thus, our conclusions may not be entirely transferrable to home sleep. Still, whenever possible, we specifically selected either the second or third nights of recording to reduce potential first-night effects, and excluded nights were patients were purposely requested to restrict their sleep time. This was also done by prior studies performed in an EMU setting [2,3].

While the EMU is generally a convenient environment to recruit subjects for clinical studies, we must mention that recruitment was more difficult than expected, especially for epilepsy patients; among the 10 decliners, 8 had epilepsy (most often, they declined because they were feeling overwhelmed). Given our small sample size, we could not divide the PNES group according to diagnostic certainty (documented and probable). Moreover, extensive psychiatric evaluations were not performed in all epilepsy subjects, and as psychiatric scales were not administered as part of this research study, only a limited subset of PNES subjects had this data. Still, we found interesting exploratory associations between psychiatric symptoms and sleep measures. Future work in a larger group of documented PNES with extensive sleep and psychiatric examinations should be undertaken to confirm our findings. Finally, it is possible that our sleep measures were influenced by seizure medications, as certain AEDs as well as others (such as benzodiazepines and antidepressants) may affect sleep (qualitatively and quantitatively). Group comparison in subjects without AEDs was limited by our small sample size and the study setting (most patients admitted to the EMU are drug-resistant); only 5 subjects with PNES were not taking AEDs, whereas all epilepsy subjects were on at least one AED. For similar reasons, it was not possible to determine the effects of benzodiazepine

or antidepressant use on sleep measures in our sample. Yet, these medications were not withdrawn during the study, thus limiting any sleep rebound effects. As sleep architecture was globally similar between subjects with PNES and epilepsy, the potential influence of AEDs or other medications on sleep appears somehow limited or non-significant in our study sample.

This pilot study comprehensively assessed both subjective (validated sleep questionnaires) and objective (EEG, actigraphy) sleep-wake patterns in PNES subjects in comparison to epilepsy controls. Our results highlight the need for clinicians to address sleep complaints and screen for insomnia in patients with PNES, as effective psychological and behavioral treatments are available and may improve overall health. Based on our findings, adding a sleep medication may not be the optimal treatment avenue for this population, and should rather be used in combination with psychological interventions. In addition, many people find it easier to talk about sleep difficulties than mental health issues, and to accept and follow up treatment for sleep. This could be a fruitful area for future research.

Funding

This study was supported by the Endowed A.J. Trustey Epilepsy Research Fund and the Canadian Institutes of Health Research (Scholarship to VL).

Declaration of interest

This study was supported by the Endowed A.J. Trustey Epilepsy Research Fund and the Canadian Institutes of Health Research (Scholarship to VL). Dr. Latreille also received financial support from Biomobie Inc. Dr. Dworetzky consults for SleepMed and Best Doctors by performing EEG interpretation and clinical second opinion consultations. Dr. Baslet has nothing to disclose. Dr. Pavlova is supported by grants from Lundbeck Inc. and Biomobie Inc.

Acknowledgments

The authors wish to thank the Brigham and Women's Hospital Division of Epilepsy for providing support and assistance with this study and all patients for their participation.

References

[1] Latreille V, Baslet G, Sarkis R, Pavlova M, Dworetzky BA. Sleep in psychogenic nonepileptic seizures: time to raise a red flag. Epilepsy Behav 2018;86:6–8. https://doi.org/10.1016/j.yebeh.2018.07.001.

[2] Bazil CW, Legros B, Kenny E. Sleep structure in patients with psychogenic nonepileptic seizures. Epilepsy Behav 2003;4:395–8. https://doi.org/10.1016/S1525-5050(03)00120-3.

[3] Popkirov S, Stone J, Derry CP. Abnormal sleep in patients with epileptic or dissociative (non-epileptic) seizures: a polysomnography study. Eur J Neurol 2018:0–1. https://doi.org/10.1111/ene.13798.

[4] Lafrance WC, Baker GA, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. Epilepsia 2013;54:2005–18. https://doi.org/10.1111/epi.12356.

[5] Iber C, Ancoli-Israel S, Chesson A, Quan S. The AASM manual for the scoring of sleep and associates events: rules, terminology and technical specifications. 2007.

[6] Pareés I, Saifee TA, Kassavetis P, Kojovic M, Rubio-Agusti I, Rothwell JC, et al. Believing is perceiving: mismatch between self-report and actigraphy in psychogenic tremor. Brain 2012;135:117–23. https://doi.org/10.1093/brain/awr292.

[7] Phillips MCL, Costello CA, White EJ, Smit M, Carino J, Strawhorn A, et al. Routine polysomnography in an epilepsy monitoring unit. Epilepsy Res 2013;105:401–4. https://doi.org/10.1016/j.eplepsyres.2013.02.015.

[8] Graham CD, Kyle SD. A preliminary investigation of sleep quality in functional neurological disorders: poor sleep appears common, and is associated with functional impairment. J Neurol Sci 2017;378:163–6. https://doi.org/10.1016/j.jns.2017.05.021.

[9] Baslet G, Dworetzky B, Perez DL, Oser M. Treatment of psychogenic nonepileptic seizures: updated review and findings from a mindfulness-based intervention case series. Clin EEG Neurosci 2015. https://doi.org/10.1177/1550059414557025.

[10] Wang Y-Y, Wang F, Zheng W, Zhang L, Ng CH, Ungvari GS, et al. Mindfulness-based interventions for insomnia: a meta-analysis of randomized controlled trials. Behav Sleep Med 2018;00:1–9. https://doi.org/10.1080/15402002.2018.1518228.