Heliyon 10 (2024) e25904

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

A polysomnographic study of slow-wave sleep loss in elderly patients with epilepsy

Sihang Wang (王思航)[1], Meina Wu (吴美娜)[1], Sangru Wu (吴桑茹), Fang Lin (林芳), Xiaolin Ji (季晓林), Jinzhu Yan (严金柱)[*]

Department of Neurology and Sleep Medical Center, Fujian Provincial Governmental Hospital, Fuzhou, China

A R T I C L E I N F O

Keywords:
Slow-wave sleep loss
Elderly
Epilepsy
Polysomnography
Spontaneous arousal index
Oxygen desaturation index

A B S T R A C T

Objective: The primary objective is to explore what causes slow-wave sleep loss in elderly patients with epilepsy. The secondary objective is to identify the PSG characteristics in elderly patients with epilepsy. The clinical demographics, sleep architecture, sleep-related events, and interictal epileptiform discharges are to be evaluated in the objectives.

Methods: The video electroencephalography (VEEG) and polysomnogram (PSG) data from 44 elderly patients with epilepsy and 52 elderly patients with sleep disorders but without definite central nervous system diseases were analysed. This was a case-control study. The differences in the PSG sleep architecture parameters (total sleep time (TST), sleep efficiency, wake after sleep onset, etc.) and sleep-related events (apnea hypopnea index, oxygen desaturation index (ODI), periodic limb movement index, etc.) between the epilepsy and control groups. As Additionally, these parameters were assessed within the elderly patients with epilepsy, comparing the slow-wave sleep existence and slow-wave sleep loss groups, using VEEG and PSG.

Results: The epileptic group exhibited significantly lower TST (343.477 ± 96.3046min vs 389.115 ± 61.5727min, $p < 0.05$), rapid eye movement (%) (13.011 ± 7.5384 vs 16.992 ± 6.7025, $p < 0.05$), non-rapid eye movement stage 3 (%) (1.35[0,7.225] vs 3.65[0.425,13.75], $p < 0.05$), and sleep efficiency (%) (69.482 ± 14.1771% vs 77.242 ± 10.6171%, $p < 0.05$). Conversely, the ODI (25.6[9.825,51.775] events/hour vs 16.85[5.3,30.425] events/hour, $p < 0.05$) and spontaneous arousal index (4.0455[2.1805,6.9609] events/hour vs 2.9709[1.4747,5.0554] events/hour, $p < 0.05$) were significantly higher in elderly patients with epilepsy. The prevalence of obstructive sleep apnea-hypopnea syndrome (OSAHS) was significantly higher in the slow-wave sleep loss group than in the slow-wave sleep existence group (100% vs 77.8%, $p < 0.05$). The incidence of slow-wave sleep loss was lower in patients with epilepsy aged between 75 and 85 years compared to those aged between 65 and 75 years.

Conclusion: Elderly patients with epilepsy exhibit higher levels of ODI and spontaneous arousal index. Our findings indicate that OSAHS could be a contributing factor to slow-wave sleep loss in this population. The incidence of slow-wave sleep loss was lower in patients aged above 75 years among elderly patients with epilepsy.

* Corresponding author. Department of Neurology and Sleep Medical Center, Fujian Provincial Governmental Hospital, Fuzhou, China.
E-mail address: yanjinzhu@fjmu.edu.cn (J. Yan).
[1] co-first author: these authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e25904
Received 21 June 2023; Received in revised form 2 January 2024; Accepted 5 February 2024
Available online 10 February 2024

1. Introduction

Epilepsy is a common nervous system disease affecting approximately 70 million people globally [1]. The prevalence rate of epilepsy in the Chinese population has more than doubled from 1990 to 2015 [2]. The age of onset in patients with epilepsy exhibits a "U-shaped" distribution, with a higher incidence in individuals aged <10 years and those aged >50 years [3]. Patients with epilepsy often suffer from sleep disorders.

Sleep disorders and epilepsy can interact with each other. Sleep deprivation more frequently results in seizures in the case of generalised epilepsies [4]. In contrast, the relationship between insufficient sleep and seizure risk of focal epilepsy is not clear, based on a previous systematic review [5]. Nevertheless, a recent study in focal epilepsy suggests that increasing sleep duration by 1.6 h may decrease the risk of seizure occurrence by 27% in the following 48 h [6]. On the other hand, the systematic review by Sudbrack et al. [7] reported that epilepsy is associated with changes in sleep, but not all patients complain of poor sleep quality due to sleep misperception in patients with epilepsy [8]. Therefore, objective polysomnogram (PSG) testing in patients with epilepsy is important. Patients with epilepsy are more prone to insomnia, sleep fragmentation, post-arousal fatigue, and parasomnia [9,10]. Therefore, there is a need to identify sleep disorders in patients with epilepsy to improve their sleep quality and reduce the frequency of epileptic seizures.

Epilepsy is closely related to non-rapid eye movement (NREM) sleep, and both experimental and clinical evidence have demonstrated that many types of epileptic seizures tend to occur during the slow-wave sleep phase [11]. Steriade et al. suggested that the slow-wave oscillations during slow-wave sleep can develop into spike waves, potentially leading to epileptic seizures and absence seizures in Lennox-Gastaut syndrome [12]. Yeh et al. conducted a meta-analysis to explore sleep macrostructure in PSG among adult patients with epilepsy and healthy controls. They found that adult patients with generalised epilepsy have increased slow-wave sleep (NREM stage 3 (N3)) [13]. However, there has been limited research on the PSG characteristics of sleep architecture and sleep-related events in elderly patients with epilepsy. While seizures are typically unpredictable and rare, electrical recordings from individuals with epilepsy often display interictal epileptiform discharges (IEDs) between seizures [14]. IEDs are most active during NREM sleep, with the highest rates during slow-wave sleep and are least likely to occur during rapid eye movement (REM) sleep [15]. Despite this close association between IEDs and sleep, reports on the effects of IEDs on sleep architecture and sleep-related events are rare. Furthermore, IEDs have been implicated in the development of cognitive deficits [16]. Research conducted in rat models of temporal lobe epilepsy have revealed that IEDs compete with physiological ripples and disrupt communication between the hippocampus and the medial prefrontal cortex during NREM sleep, thereby impairing memory consolidation [17]. However, slow-wave sleep, which is closely associated with IEDs (IED rates were highest in the slow-wave sleep) exerts an inverse impact on cognitive function. Slow-wave sleep causally enhances cognitive function in older adults and individuals with mild cognitive impairment [18]. Studies have also indicated [19] that the loss of slow-wave sleep may accelerate brain aging and mild brain injury. Conversely, accelerating brain aging and mild brain injury can reduce the brain's ability to generate slow-wave sleep, eventually leading to poor cognitive function in elderly patients with epilepsy. The critical question arises: what causes slow-wave sleep loss, IED, or other aspects of sleep architecture and sleep related events? Our study aims to address this question, establishing an electrophysiological foundation for future investigations into the association between epilepsy and cognitive impairment. Furthermore, it provides preliminary insights into strategies for enhancing slow-wave sleep.

In this study, the primary objective is to identify potential influencing factors leading to slow-wave sleep loss in elderly patients with epilepsy, the sleep architecture, sleep-related events, and IED index in elderly patients with epilepsy and slow-wave sleep loss are to be identified in this objective. The secondary objective of our study is to explore the PSG characteristics in elderly patients with epilepsy, the clinical demographics, the sleep architecture, and sleep-related events in elderly patients with epilepsy are to be identified in this objective. So, we compared the clinical demographic, and sleep architecture characteristics between elderly patients with epilepsy and IEDs and those presenting with sleep disorders but without definite central nervous system diseases. In addition, we compared the sleep architecture and sleep-related events in elderly patients with epilepsy with or without slow-wave sleep loss to identify potential influencing factors leading to slow-wave sleep loss in patients with epilepsy.

2. Materials and methods

2.1. Data acquisition and evaluation criteria

This was a case-control study conducted at the Department of Neurology and Sleep Medicine Centre of Fujian Provincial Governmental Hospital from March 2018 to September 2022. The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all study subjects. Patients attending the outpatient or inpatient departments of Fujian Provincial Governmental Hospital were recruited for this study as part of epilepsy group if they fulfilled the following inclusion criteria: (1) Age >65 years; (2) a confirmed diagnosis of epilepsy based on the 2017 diagnostic criteria for epilepsy established by the International League Against Epilepsy [20]; and (3) detection of IEDs during overnight PSG monitoring, characterised by the typical epileptic waveform, including sharp, spiked, or spiked-sharp-slow wave complexes. Exclusion criteria included: (1) Consumption of alcohol, coffee, or drugs affecting sleep (except antiepileptic drugs (AEDs)) within the last 2 weeks; (2) presence of mental disorders, circulatory disorders, or other diseases affecting sleep; (3) inability to cooperate with the examination; (4) experience of epileptic seizures during PSG monitoring; and/or (5) diagnosis of a specific epilepsy syndrome. Within the epilepsy group, patients were further divided into two subgroups: the slow-wave sleep existence group (comprising patients with slow-wave sleep) and the slow-wave sleep loss group (comprising patients with no slow-wave sleep). A control group was also recruited, consisting of patients with sleep

disorders but without definite central nervous system diseases from the outpatient or inpatient departments of the Fujian Provincial Governmental Hospital during the same period. Exclusion criteria for controls included: (1) Consumption of alcohol, coffee, or drugs affecting sleep within the last 2 weeks; (2) presence of mental disorders, circulatory disorders, or other diseases affecting sleep; and/or (3) inability to cooperate with the examination. Controls were recruited from the Department of Neurology and Sleep Medicine Center of Fujian Provincial Governmental Hospital after seeking medical attention. The number of healthy controls fell short of the required sample size, thus precluding the inclusion of a healthy control group.

2.2. Instruments

Continuous overnight synchronous monitoring of nocturnal sleep architecture and sleep-related events was conducted on both the epilepsy and control groups using a 16-channel video electroencephalography (VEEG) and PSG.

Montage PSG was performed with the Philips Alice 6 LDxS (Philips, Pennsylvania, USA) using the following montage: 16 electroencephalogram (EEG) channels (Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1, O2, 200 Hz, filter: low-pass 0.3 Hz, high-pass 35 Hz), two electro-oculogram (EOG) channels (1 cm below and 1 cm lateral of the outer right canthus as well as 1 cm above and 1 cm lateral of the outer left outer canthus, 200 Hz, filter: low-pass 0.3 Hz, high-pass 35 Hz), 3 electromyogram (EMG) channels (Chin, left leg, and right leg, 200 Hz, filter: low-pass 10 Hz, high-pass 100 Hz), 6 electrocardiogram (ECG) channels (ECG1, ECG2, III, aVR, aVL, aVF, 200 Hz, filter: low-pass 0.3 Hz, high-pass 70 Hz), a snoring channel (microphone, 500 Hz, filter: low-pass 10 Hz, high-pass 100 Hz), oronasal airflow (200 Hz, filter: low-pass 0.03 Hz, high-pass 100 Hz), thoracic and abdominal respiratory effort channels (inductance plethysmography belt, 200 Hz, filter: low-pass 0.1 Hz, high-pass 15 Hz), finger photoplethysmography (non-dominant arm, 200 Hz), and body position (recorded every 30 s).

Sleep parameters were calculated using the Sleepware G3 software (Philips, Pennsylvania, USA) (Table 1). An A/D conversion amplifier with an amplification factor of 12 was used to process the signal.

2.3. Measurements

All participants were instructed to discontinue the use of drugs that might affect sleep (except AEDs used by patients with epilepsy) for two weeks before the examination. Participants were also familiarised with the sleep monitoring environment, examination purpose, and techniques to relieve tension. During the examinations, electrodes were positioned, and the impedance of the electrodes wasverified. Analysis of PSG data was conducted in 30 s epochs by two trained, independent, and blinded raters, according to the guidelines outlined in the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events: Rules, Terminology, and Technical Specifications version 2.3 [21]. In cases where sleep efficiency differed by $\leq$ 5% between raters, the mean of each quantitative sleep parameter from both raters was used for analysis. In cases where sleep efficiency differed by $>$ 5% between raters, a consensus scoring was reached through evaluation by a third rater who was blinded to allocation and previous ratings. Inter-rater reliability, determined by intraclass correlation, based on the scoring of the first two raters was provided for the primary outcome. The presence or absence of epileptic seizures and related behaviours during sleep were monitored by synchronous infrared video recording. The presence or absence of epileptic seizures or IEDs during sleep in VEEG was evaluated by manual analysis in 10 s epochs. Both VEEG and PSG data were reviewed by the same investigator. Sleep status was scored according to the AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology, and Technical Specifications version 2.3 [21].

2.4. Assessment of sleep-related events

Respiration-related events were determined by oronasal airflow, thoracoabdominal respiration, thermal sensor, and index finger

Table 1
Sleep parameters.

Sleep parameter	Definition
Time in bed (TIB)	Time in bed between the lights-off and lights-on markers
Sleep latency	Time between lights-off marker and first epoch of any sleep stage
Total sleep time (TST)	Time asleep (in any sleep stage) within TIB (min) TST = NREM sleep stage 1 (N1) + NREM sleep stage 2 (N2) + N3 + REM
N1%	Stage 1 (in minutes and % TST)
N2 %	Stage 2 (in minutes and % TST)
N3 %	Stage 3 (in minutes and % TST)
REM%	Rapid eye movement (in minutes and % TST)
Sleep efficiency	Percentage of sleep while in bed (%) SE = (TST/TIB) × 100
Wake after sleep onset (WASO)	Time awake after first sleep episode (min) WASO = TIB - Sleep latency - TST
Arousal index	Arousal index = Times of arousal/TST (h)
Respiration arousal index	Respiration arousal index = Times of arousal (caused by respiration events)/TST (h)
Leg movement arousal index	Leg movement arousal index = Times of arousal (caused by leg movement)/TST (h)
Spontaneous arousal index	Spontaneous arousal index = Times of arousal (unknown cause)/TST (h)

oxygen saturation.

Periodic limb movement disorder (PLMD) and REM sleep disorder were determined by EEG, submental EMG, and leg movement. Sleep status scoring used a 30 s/frame time window, while EEG analysis used a 10 s/frame time window.

The onset of respiration-related events such as apnea, hypopnea, obstructive apnea, central apnea, and mixed apnea during sleep was determined according to the following criteria: apnea was defined as a minimum of a 90% decrease in the peak of the thermal sensor signal from the pre-event baseline for at least 10 s; hypopnea was defined as a minimum of a 30% decrease in the peak respiratory airflow signal from baseline for at least 10 s and a decrease in oxygen saturation of at least 3% from the pre-event baseline or following an arousal event; obstructive apnea was defined as a sustained or gradually increased inspiratory effort throughout sleep due to a loss of airflow; Conversely, central apnea was defined as the absence of an inspiratory effort throughout sleep following the loss of airflow; and mixed apnea was confirmed if the inspiratory effort was initially absent throughout the loss of airflow but became present later in the event. The apnea hypopnea index (AHI) was calculated by counting the total number of apnea and hypopnea episodes per hour during one overnight sleep. A diagnosis of obstructive sleep apnea-hypopnea syndrome (OSAHS) was established if there were 30 more repeated attacks of obstructive apnea and hypopnea during a 7-h sleep every night or an AHI of more than 5 times per hour.

The criteria for PLMD were as follows: an adult periodic limb movement index (PLMI) during sleep exceeding 15 times/h, resulting in significant sleep disturbance; psychological, physical, social, occupational, educational, or behavioural dysfunction; or other important functional impairment. Moreover, the presence of other sleep disorders, medical or neurological diseases, or psychiatric disorders that could cause these symptoms was excluded [21].

The criteria for REM sleep behaviour disorder (RBD) [21] included recurrent sleep-related vocalizations and complex movements; abnormal behaviour in REM sleep, either confirmed by PSG or inferred based on dream enactment history; REM sleep without atonia (RWA); and the absence of other sleep or psychiatric disorder, as well as drug and substance use, that could explain these symptoms. RWA was defined as meeting the criteria for REM sleep were EEG and EOG, but with achalasia in the submental or anterior fibular EMG. These EMG activities were classified as either tonic or temporal activities. Tonic activity occurred when at least 50% of the submental EMG amplitude per frame (30 s) was higher than the minimum amplitude during NREM sleep time. The temporal activity was determined by dividing each frame (30 s) of the REM sleep into 10 smaller frames (3 s). Temporal activity was considered present if at least 5 of the 10 frames presented an EMG burst with transient activity for about 0.1–5 s, and the EMG amplitude was at least 4 times higher than the background activity.

2.5. Statistical analysis

The statistical package for the social sciences software (SPSS) version 26.0 was used to analyse the data. Differences in PSG and VEEG parameters were compared between the epilepsy and control groups, as well as between the slow-wave sleep existence group and slow-wave sleep loss groups. All continuous variables were tested for normality using Levene's test for homogeneity of variance. The *t*-test was used to compare variables with homogeneity of variance, while the rank sum test was used to compare variables with a significantly abnormal distribution and heterogeneity of variance. Binary logistic regression analysis was conducted to identify potential influencing factors for slow-wave sleep loss. The Chi-squared (χ^2) test was used to compare categorical variables. For all statistical tests, a p-value below 0.05 was considered statistically significant.

Table 2
Comparison of demographic and clinical data between the epilepsy group and control group.

	Epilepsy group(n = 44)	Control group(n = 52)	Z/t/X2	P
Age(years)	77[68.25,83]	72[66.25,76.75]	−1.863	0.062
BMI(kg/㎡)	23.25[21.1,24.8]	23.3[21.125,26.15]	−0.173	0.863
Gender			1.336	0.248
Male	28 (63.6)	27 (51.9)		
Female	16 (36.4)	25 (48.1)		
Comorbidities hypertension	20 (45.5)	27 (51.9)	0.399	0.528
Comorbidities diabetes	10 (22.7)	7 (13.5)	0.518	0.472
Etiology				
Structural	7 (15.9)			
Genetic	1 (2.3)			
Infectious	0 (0)			
Metabolic	1 (2.3)			
Immune	0 (0)			
Unknown	35 (79.5)			
Epilepsy types				
Focal(temporal)	5 (11.4)			
Focal(extra-temporal)	23 (52.3)			
Generalised	4 (9.1)			
Unknown	12 (27.2)			

BMI: body mass index; N, number; Statistics presented as median [P25, P75] or N (%).

3. Results

3.1. Characteristics of the participants

Among the 44 elderly patients with epilepsy included in the study, 28 were males (63.6%), and 16 were females (36.4%). The mean age of the patients was 77 [68.25, 83] years, and the mean disease duration was 0.5 [0.04, 2] years. The majority (n = 28, 63.6%) of the patients were diagnosed with focal epilepsy, four cases (9.1%) had generalised epilepsy, and 12 cases (27.3%) had epilepsy of unknown origin. Eight patients used AEDs but did not use sedatives, hypnotics, or other stimulant drugs. Among the eight patients treated with AEDs, six were receiving monotherapy, including oxcarbazepine (n = 3), levetiracetam (n = 1), or carbamazepine (n = 1), and two patients were receiving combination of therapies, including topiramate with clonazepam (n = 1) or valproate sodium with gabapentin (n = 1).

In the control group, 27 were males (51.9%), and 25 were females (48.1%). The mean age of the control group was 72 [66.25, 76.75] years. None of these patients used sedatives, hypnotics, or other drugs that affect sleep.

There were no statistically significant differences in age, gender, body mass index (BMI), and comorbidities (hypertension and diabetes) between the elderly patients with epilepsy and those without epilepsy ($p > 0.05$). The clinical and demographic characteristics of the participants are summarized in Table 2.

3.2. Comparison of sleep architecture and sleep-related events between the epilepsy and control groups

When compared to individuals in the control group, the elderly patients with epilepsy exhibited significantly lower TST, REM percentage (%), N3 percentage (%), and sleep efficiency. Conversely, the oxygen desaturation index (ODI) and spontaneous arousal index were significantly higher in the epilepsy group. The remaining PSG parameters and sleep-related events (OSAHS, PLMD, and RBD) did not differ significantly between the two groups (Table 3).

3.3. Comparison of clinical and demographic information, sleep architecture, and sleep-related events between the slow-wave sleep loss and slow-wave sleep existence groups in the elderly patients with epilepsy

No statistically significant differences were found in the demographic and clinical data between the slow-wave sleep loss and slow-wave sleep existence groups in the elderly patients with epilepsy (Table 4).

However, the slow-wave sleep loss group exhibited a significantly higher N1 percentage (%) and lower REM percentage (%). The prevalence of OSAHS was significantly higher in the slow-wave sleep loss group than in the slow-wave sleep existence group. No statistically significant differences were found in the other sleep architectures and sleep-related events between the two groups (Table 5).

Table 3
Comparison of the PSG parameters and sleep-related events between the epilepsy and control groups.

	Epilepsy group(n = 44)	Control group(n = 52)	Z/t	P
Sleep latency (min)	15.750[7,20.875]	14.250[5.625,24.375]	−0.114	0.909
N1%	20.2[13.1,27.875]	15.2[11.325,24.6]	−1.894	0.058
N1 duration (min)	61.750[45.125, 100.500]	61.500[44.750, 92.750]	−0.500	0.617
N2 %	58.552 ± 11.6414	58.046 ± 10.1673	−0.227	0.821
N2 duration (min)	202.125 ± 74.0756	226.144 ± 53.1722	−1.844	0.068
N3 %	1.35[0,7.225]	3.65[0.425,13.75]	−2.039	0.041**
N3 duration (min)	3.5[0, 29.0]	15.000[1.625, 46.625]	−2.069	0.039**
REM%	13.011 ± 7.5384	16.992 ± 6.7025	2.738	0.007*
REM sleep duration (min)	45.000[19.500, 62.375]	65.500[48.375, 83.000]	−3.651	0.0001**
TST (min)	343.477 ± 96.3046	389.115 ± 61.5727	2.71	0.008*
Sleep efficiency (%)	69.482 ± 14.1771	77.242 ± 10.6171	2.99	0.004*
WASO (min)	131.25[95.25,227.875]	119.5[76.75,155.125]	−1.647	0.1
Arousal index (events/hour)	13.95[7.4,18.65]	10.85[6.2,15.75]	−1.504	0.133
Respiration arousal index (events/hour)	0.5124[0.1822,1.5257]	0.8197[0.2107,1.5683]	−1.001	0.317
Leg movement arousal index (events/hour)	2.0814[0.8216.3.6689]	2.0160[1.1635,2.9906]	−0.331	0.741
Spontaneous arousal index (events/hour)	4.0455[2.1805,6.9609]	2.9709[1.4747,5.0554]	−2.25	0.024**
OSAHS	38 (86.4)	43 (82.7)	0.244	0.622
AHI (events/hour)	24.85[8.075,45.875]	18.4[6.875,27.7]	−1.875	0.061
Mean oxygen saturation (%)	94[92,94]	94[93,95]	−1.125	0.26
ODI (events/hour)	25.6[9.825,51.775]	16.85[5.3,30.425]	−1.971	0.049**
PLMD	18 (40.9)	26 (50)	0.793	0.373
PLMI (events/hour)	9.9[0,26.5]	13.4[4.05,36.025]	−1.72	0.085
RBD	5 (11.4)	7 (13.5)	0.096	0.757

*t-test: $p < 0.05$, **Mann-Whitney U rank sum test: $p < 0.05$. SD: standard deviation; PSG: polysomnography, N1: NREM sleep stage 1, N2: NREM sleep stage 2, N3: NREM sleep stage 3, REM: rapid eye movement, OSAHS: obstructive sleep apnea-hypopnea syndrome, PLMD: periodic limb movement disorder, RBD: rapid eye movement sleep behavior disorder. Statistics presented as mean ± SD, median [P25, P75] or N (%).

Table 4
Comparison of demographic and clinical data between the slow-wave sleep existence and the slow-wave sleep loss groups in the elderly patients with epilepsy.

	Slow-wave sleep loss group(n = 17)	Slow-wave sleep existence group(n = 27)	Z/t/X2	P
Duration (years)	0.5[0.03,4]	1[0.04,2]	−0.473	0.636
BMI	22.9[21.4,25.25]	23.6[20.8,24.8]	−0.422	0.673
Age	76.29 ± 9.299	76.33 ± 7.54	−0.015	0.988
Gender			1.972	0.160
Male	13 (76.5)	15 (55.6)		
Female	4 (23.5)	12 (44.4)		
Comorbidities hypertension	10 (58.8)	10 (37)	1.997	0.158
Comorbidities diabetes	2 (11.8)	8 (29.6)	1.896	0.169
Taking AEDs	4 (23.5)	4 (14.8)	0.522	0.470
Types of AEDs			1.063	0.588
0	13 (76.5)	23 (85.2)		
1	3 (17.6)	2 (7.4)		
2	1 (5.9)	2 (7.4)		

Statistics presented as mean ± SD, median [P25, P75] or N (%).

Table 5
Comparison of the sleep parameters between the slow-wave sleep existence and slow-wave sleep loss groups in the elderly patients with epilepsy.

	Slow-wave sleep loss group (n = 17)	Slow-wave sleep existence group (n = 27)	Z/t	P
Sleep latency (min)	13[6,24.25]	16 [,7, 21]	−0.398	0.691
N1 %	27.2[17.75,41.15]	18.6[12.3,24]	−2.519	0.012**
N1 duration (min)	93.618 ± 61.8652	66.074 ± 29.6786	1.716	0.101
N2 %	59.6 ± 13.5142	57.893 ± 10.5154	0.469	0.641
N2 duration (min)	192.059 ± 96.0490	208.463 ± 57.3570	−0.636	0.531
REM %	10.182 ± 7.4725	14.793 ± 7.148	−2.047	0.047*
REM sleep duration (min)	36.50[7.25, 48.75]	50[34, 68]	−2.338	0.019**
TST (min)	317.794 ± 117.204	359.648 ± 78.6287	−1.42	0.163
Sleep efficiency (%)	67.1[58.7,75.75]	76.9[63.7,82.1]	−1.482	0.138
WASO (min)	142.5[91,235.25]	109.5[95,207.5]	−0.518	0.604
Arousal index (events/hour)	18.1[7.15,28.15]	12.2[7.3,17.1]	−1.723	0.085
Respiration arousal index (events/hour)	1.0676[0.2346,1.8214]	0.4225[0.1727,1.0330]	−1.351	0.177
Leg movement arousal index (events/hour)	2.1270[0.7985,4.8830]	2.0357[0.9549,3.6052]	−0.301	0.763
Spontaneous arousal index (events/hour)	3.5722[1.9684,7.2025]	4.4860[2.3841,6.9704]	−0.518	0.604
OSAHS			4.374	0.036***
without(AHI < 5 events/hour)	0 (0)	6 (22.2)		
with(AHI≥5 events/hour)	17 (100)	21 (77.8)		
AHI (events/hour)	36.2[9.25,61.15]	22[6.4,39.6]	−1.29	0.197
Mean oxygen saturation (%)	93[92,94]	94[92,95]	−0.555	0.579
ODI (events/hour)	29[10.6,60.35]	21.6[8.2,46.8]	−1	0.317
PLMD	8 (47.1)	10 (37)	0.433	0.510
PLMI (events/hour)	9.3[0,54.2]	10[0.9,18.3]	−0.511	0.609
RBD	2 (11.8)	3 (11.1)	0.004	0.947
IED index	0.97[0.17, 7.57]	1.04[0.17, 3.98]	−0.301	0.763

*t-test: $p < 0.05$, **Mann-Whitney U rank sum test: $p < 0.05$, ***χ^2 test: $p < 0.05$ Statistics presented as mean ± SD, median [P25, P75] or N (%).

3.4. Impact of gender, age, PLMD, mean oxygen saturation, and OSAHS on the incidence of slow-wave sleep loss within patients in the epilepsy group

We included gender, age, PLMD, mean oxygen saturation and OSAHS to construct a multifactor logistic regression analysis. Patients with epilepsy aged between 75 and 85 years had a significantly lower incidence of slow-wave sleep loss than those aged between 65 and 75 years (OR: 0.113, 95%CI 0.016–0.791, P = 0.028, Table 6).

4. Discussion

Epilepsy is closely associated with NREM sleep. During NREM sleep, neurons in the brain stem, thalamus, and cortex discharge synchronously, generating IEDs. These IEDs cause repeated arousals and sleep fragmentation, leading to intermittent daytime sleepiness and potentially triggering epileptic seizures and epileptiform discharges, thus forming a vicious cycle [22]. N3, which is an important component of NREM sleep, occupies a larger proportion of sleep time compared to REM sleep [23]. However, the effects of IEDs on sleep architecture and sleep-related events in the elderly, as well as the influencing factors for slow-wave sleep loss in elderly patients with epilepsy, have rarely been reported.

As reported in the literature, children with epilepsy have a significantly longer N2 percentage and decreased sleep efficiency [24],

Table 6
Logistic regression analysis evaluating the impact of gender, age, PLMD, mean oxygen saturation, and OSAHS on the incidence of slow-wave sleep loss in the epilepsy group.

	OR	95%CI	P
Gender			
Male	1		
Female	0.337	0.063–1.82	0.206
Age			
65–75 years old	1		
75–85 years old	0.113	0.016–0.791	0.028*
85–95 years old	2.228	0.357–13.898	0.391
PLMD			
without	1		
with	2.055	0.438–9.635	0.361
mean oxygen saturation			
85–90%	1		
90–95%	0.613	0.025–15.063	0.764
95–100%	0.371	0.012–11.697	0.573
OSAHS			
without	1		
with	2.31	0.461–11.583	0.309

*$p < 0.05$.

while adults with nocturnal frontal lobe epilepsy have increased WASO [7] and shorter REM sleep [25]. In this study, the results showed that elderly patients with epilepsy had decreased TST, REM percentage (%), N3 percentage (%), and sleep efficiency, with the N3 percentage (%) differing from previous findings. Previous studies have shown that poor sleep quality and daytime sleepiness in patients with nocturnal frontal lobe epilepsy can trigger epileptic seizures and IEDs [26]. Interictal epileptiform activity in juvenile myoclonic epilepsy may increase arousal duration and sleep onset latency, and decrease sleep efficiency [27]. Based on the results of our study, we speculate that IEDs were the key factor leading to decreased TST and sleep efficiency in patients with epilepsy. Yeh et al. [13] found that adult patients with epilepsy exhibit increased slow-wave sleep; however, their investigation was limited to generalised epilepsy, whereas our study only included four (9.1%) patients with generalised epilepsy. Other studies have attributed the reduction in N3 to antiepileptic therapies [28], the cognitive status of the child [29], or the first night effect [30]. The majority of these studies focused on drug-resistant epilepsy or epilepsy in individuals below the elderly age group. However, our study focused on the elderly individuals with epilepsy, and there is currently no existing literature demonstrating a reduction in N3 (slow-wave sleep) among this population. We speculate that the reduction in N3 observed in this study may potentially be attributed to IEDs. IEDs are closely associated with pathological high-frequency oscillations (HFOs), which jointly influence changes in slow-wave sleep. Previous studies [15,31] reported that the incidence rates of IEDs and HFOs are highest during slow-wave sleep, leading to frequent arousal of patients with epilepsy during this sleep stage. As a result, the duration of slow-wave sleep time gradually shortens, and the time spent in REM sleep is reduced, ultimately altering the sleep architecture of elderly patients with epilepsy. Interestingly, no statistically significant differences were found in the IED index between the slow-wave sleep loss and slow-wave sleep existence groups in the elderly patients with epilepsy. We speculate that this lack of difference is due to the diminishing influence of IEDs on slow-wave sleep with increasing age [32]. Furthermore, our study found that the spontaneous microarousal index was higher in elderly patients with epilepsy compared with the control group. However, the relationship between this parameter and epilepsy is rarely reported in the literature. The spontaneous microarousal index has been associated with disrupted sleep continuity and sleep fragmentation in previous studies [33], as well as heightened autonomic nerve excitability after accounting for the influence of respiration, snoring, and leg movement [34]. Patients with epilepsy often experience potential autonomic dysfunction and epileptic seizures, which can spread to autonomic nerve control center, such as specific areas of the brain stem and subcallosal areas, resulting in acute heart and respiratory problems [35]. Recent studies have shown that epilepsy can damage the autonomic nerve during the ictal, interictal, and post-ictal phases [36,37], with this nerve damage being associated with sudden death in patients with epilepsy. Gloor et al. demonstrated in feline models that intramuscular injection of penicillin induced spike discharges from spindle rhythms in NREM sleep, leading to relative neuronal synchronisation and the promotion of epileptic seizures [38]. It has also been proven among patients with epilepsy that IEDs are activated to the maximum extent during slow-wave sleep but decline during REM sleep [39]. Recently, Malow et al. [40] suggested that NREM sleep initiation and maintenance contribute more to partial epileptic seizures than REM sleep and arousal-related processes. However, most existing studies are limited to temporal lobe epilepsy. In our study, the elderly epilepsy group experienced a decreased percentage of sleep loss (39%) during slow-wave sleep compared to the control group. It is speculated that the increase in the spontaneous microarousal index in elderly patients with epilepsy may be related to slow-wave sleep and nocturnal IEDs. Nevertheless, further research is required to confirm these associations.

There is a strong correlation between OSAHS and epilepsy. A recent meta-analysis reported a prevalence rate of mild to severe OSAHS in adult patients with epilepsy of 33.4% (95%CI: 20.8–46.1%), and it found that adult patients with epilepsy are more susceptible to OSAHS than healthy controls (OR = 2.36, 95%CI: 1.33–4.18) [41]. In our study, although the incidence of OSAHS and AHI did not differ significantly between the elderly epilepsy and control groups, the ODI in the elderly epilepsy group was higher than that in the control group. One possible explanation for this could be that all the elderly patients enrolled in our study had IED during PSG, whereas those with epileptic seizures in PSG were excluded. Previous studies have shown that epileptic patients with obstructive sleep

apnea (OSA) tend to have poorly controlled epileptic seizures and are more prone to experiencing recurrent seizures [42]. Extensive and frequent IEDs can affect upper airway control during sleep [43], potentially increasing ODI. Through PSG, Natasa et al. [44] observed a significant decline in nocturnal oxygen saturation among 31 children with refractory epileptic encephalopathy and nocturnal IED, suggesting that IED may contribute to an increase in ODI. Nocturnal hypoxia resulting from increased ODI has a significant impact on the elderly. Through neuroimaging, Scullin et al. [45] found that increased nocturnal hypoxia in the elderly is associated with cortical thinning in the frontal region, which is related to slow-wave generation in the frontoparietal network associated with cognitive control. Additionally, in a study of 167 elderly individuals, Gelber et al. [46] compared PSG results before death with those of brain injury tests after death and found that those with reduced nocturnal oxygen saturation and slow-wave sleep were more likely to suffer from microinfarctions and brain atrophy. Research conducted in a northern Taiwanese population revealed an association between repetitive respiratory events with hypoxia and spontaneous arousal and cognitive dysfunction [47]. Hypoxemia can also contribute to reduced attention-executive function and verbal memory in patients with epilepsy [48]. The interaction between increased ODI, spontaneous arousal index, and slow-wave sleep loss in elderly patients with epilepsy contributes to brain aging and cognitive decline.

Slow-wave sleep is influenced by a variety of factors, but the specific factors contributing to slow-wave sleep loss in elderly patients with epilepsy have been rarely studied. A meta-analysis conducted by Ohayon et al. [49] showed that as individuals age, their sleep becomes more unstable, slow-wave sleep time gradually decreases, and the duration of N1 and N2 sleep stages increases. So, the increasing age may cause the slow-wave sleep loss in elderly patients with epilepsy. In our study, we did not observe a statistically significant relationship between the incidence of slow-wave sleep loss and age in elderly patients with epilepsy. This lack of correlation might be because our study exclusively included elderly patients with epilepsy. Furthermore, epilepsy and OSAHS often coexist [50], especially in the elderly [51]. In our study, the prevalence of OSAHS differed between the slow-wave existence sleep and slow-wave sleep loss groups in elderly patients with epilepsy. Previous studies have reported that recurrent apnea in patients with OSAHS leads to a reduction in slow-wave sleep and increased sleep fragmentation [52], ultimately resulting in slow-wave sleep loss. According to research by Miano et al. [53], the negative impact of chronic intermittent hypoxia caused by OSAHS increases the risk of IED, which is another potential contributor to slow-wave sleep loss. So, OSAHS may cause the slow-wave sleep loss in elderly patients with epilepsy.

There is a comorbid association between epilepsy and PLMD. Previous studies have indicated that [54,55] patients with epilepsy tend to experience increased periodic limb movements (PLMS) and significantly increased PLMI. However, these studies did not specifically investigate elderly patients with epilepsy. PLMD is known to affect approximately 45% of individuals aged above 65 years [56], and is caused by degeneration of the striatal dopaminergic system. The severity of PLMS is closely related to the degree of dopaminergic activity reduction. However, patients with epilepsy exhibit heightened dopaminergic activity in the brain due to recurrent epileptic seizures, which may appear contradictory to the observed increase in PLMI. Nevertheless, our study did not identify a statistically significant difference in PLMI between elderly epilepsy and control groups. This lack of significant difference could be due to the fact that dopaminergic activity in the brain is not necessarily higher in the interictal phase compared to the ictal phase. Currently, the factors influencing PLMD in elderly patients with epilepsy remain unknown and lack clinical evidence. Hardy et al. found that patients with PLMD present with decreased slow-wave sleep in comparison to good sleeper controls [57]. So, PLMD may cause the slow-wave sleep loss in elderly patients with epilepsy. Furthermore, several studies have shown that slow-wave sleep is related to age and gender. Moraes et al. [58] reported a significant decline in the percentage of slow-wave sleep with increasing age, with this decline being more pronounced in men. Conversely, Voderholzer et al. found no difference in slow-wave sleep duration between women and men [59]. So, gender may cause the slow-wave sleep loss in elderly patients with epilepsy. Recurrent apnea episodes in patients with epilepsy and OSAHS results in a continual decrease in mean oxygen saturation [52]. So, mean oxygen saturation may be a more sensitive influencing factor for slow-wave sleep loss in elderly patients with epilepsy.

Overall, factors such as age, OSAHS, PLMD, gender, and mean oxygen saturation are associated with slow-wave sleep. Therefore, in this study, we further explored the relationships between slow-wave sleep loss and age, OSAHS, PLMD, gender, and mean oxygen saturation. Our findings indicate that the probability of slow-wave sleep loss in patients with epilepsy aged between 75 and 85 years (15 cases) was lower compared to patients aged between 65 and 75 years (19 cases). This finding contrasts with previous studies that have shown a gradual decrease in slow-wave sleep with age in healthy individuals. Aanestad et al. [32] screened 10,547 patients via PSG and observed that the morphological characteristics of IEDs decreased with advancing age, resulting in lower amplitudes that were more laterally distributed. These findings suggest that as individuals age, the influence of IED on slow-wave sleep in patients with epilepsy gradually decreases, leading to a reduced likelihood of experiencing slow-wave sleep loss. However, it is important to note that our study had a relatively small sample size, which limited the statistical analysis of this association. In addition, we observed no statistically significant difference in the probability of slow-wave sleep loss between patients aged 85–95 years and those aged 65–75 years, which may be attributed to the limited number of patients aged 85–95 years (10 cases). For future research, the sample size should be further expanded to enable investigation of the correlation between slow-wave sleep loss and age in elderly patients with epilepsy.

In this study, only eight patients in the epilepsy group were undergoing treatment with AED drugs, namely, phenytoin sodium, carbamazepine, oxcarbazepine, valproate sodium, levetiracetam, topiramate, clonazepam, and gabapentin. Liguori et al. [60] reviewed the literature on the relationship between AEDs and sleep, and concluded that oxcarbazepine, carbamazepine, and levetiracetam have no impact on sleep, whereas clonazepam can cause daytime sleepiness, and valproate sodium can alter sleep. However, none of these AEDs were found to decrease the duration of slow-wave sleep. Other studies have reported that gabapentin can increase the duration of slow-wave sleep [61]. The effects of phenytoin sodium on the duration of slow-wave sleep remains controversial. Although Benjamin et al. [61] found that phenytoin sodium could potentially shorten the duration of slow-wave sleep in patients with epilepsy, it is essential to note that this study lacked a matched control group of patients of similar age for comparison. Currently, the

effect of topiramate on sleep architecture remains relatively unexplored in the existing literature. It is plausible that AEDs may have had minor impacts on sleep architecture. However, due to the small sample size in our study, it was not possible to statistically analyse the impact of AEDs on the duration of slow-wave sleep.

Our study has some limitations that have to be acknowledged. First, the distribution and differences in the frequencies of epileptiform discharges were not considered during the different sleep stages. Further studies with functional imaging data are necessary to evaluate the association between sleep disorders and IEDs in elderly patients with epilepsy. This study may exhibit potential selection bias due to the small sample size, and all data were collected from the same Sleep Medicine Centre. We lacked a healthy control group to provide a baseline for comparing sleep architecture and sleep-related events in the elderly population. Consequently, the proportion of patients with sleep disorders included in our study may not accurately represent the general population. Therefore, larger multicentre studies are recommended to improve the generalisability of the results. The impact of different AEDs on body weight and sleep architecture was not considered and hence requires further investigation. Other potential variables, such as living conditions, patient characteristics, sleep hygiene, underlying brain lesions, comorbidities, and medication interactions, could influence the results of our study and should be explored further. Additionally, due to the retrospective nature of the study, we were unable to perform cognitive assessments in our patients, which limits the interpretation of the direct link between sleep disturbances and cognitive outcomes. Future research should prioritise investigating this aspect.

5. Conclusion

When compared to the control group, elderly patients with epilepsy exhibited altered sleep architecture and sleep-related events, which manifested as decreased TST, REM percentage (%), N3 percentage (%), and sleep efficiency, along with increased ODI and spontaneous arousal index. We speculate that IEDs were the key factor leading to decreased TST, REM percentage (%), N3 percentage (%) and sleep efficiency, as well as the increased ODI and spontaneous arousal index in patients with epilepsy.

Conversely, sleep-related events (OSAHS, PLMD, and RBD) did not differ significantly between the epilepsy group and control group.

Additionally, the prevalence of OSAHS was significantly higher in the slow-wave sleep loss group than in the slow-wave sleep existence group. Patients with OSAHS leads to increased sleep fragmentation and risk of IEDs, ultimately resulting in slow-wave sleep loss.

The probability of slow-wave sleep loss in epileptic patients aged 75 to 85 was lower than that in epileptic patients aged 65–75 years. For future research, the sample size should be further expanded to enable investigation of the correlation between slow-wave sleep loss and age in elderly patients with epilepsy.

Funding

This work was supported by the Natural Science Foundation of Fujian Province, China [grant number 2019J01095].

Data availability

Data associated with this study has not been deposited into a publicly available repository. Data will be made available on request.

Ethics statement

This study was reviewed and approved by the Ethics Committee of the Fujian Provincial Governmental Hospital, with the approval number: [2019J01012090]. All patients (or their proxies/legal guardians) provided informed consent to participate in the study. All participants/patients (or their proxies/legal guardians) provided informed consent for the publication of their anonymised case details and images. The PSG and VEEG were also approved by the Ethics Committee of the Fujian Provincial Governmental Hospital.

CRediT authorship contribution statement

Sihang Wang: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Meina Wu:** Supervision, Investigation, Data curation. **Sangru Wu:** Writing – review & editing. **Fang Lin:** Investigation, Data curation. **Xiaolin Ji:** Writing – review & editing, Supervision. **Jinzhu Yan:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

All authors approved the final version of the manuscript, agree to be accountable for all aspects of the work in ensuring that

questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

References

[1] R.D. Thijs, et al., Epilepsy in adults, Lancet 393 (10172) (2019) 689–701, https://doi.org/10.1016/S0140-6736(18)32596-0.
[2] P. Song, et al., Prevalence of epilepsy in China between 1990 and 2015: a systematic review and meta-analysis, J. Glob. Health 7 (2) (2017) 020706, https://doi.org/10.7189/jogh.07.020706.
[3] B.S. Dham, K. Hunter, F. Rincon, The epidemiology of status epilepticus in the United States, Neurocritical Care 20 (3) (2014) 476–483, https://doi.org/10.1007/s12028-013-9935-x.
[4] L. Xu, et al., Juvenile myoclonic epilepsy and sleep, Epilepsy Behav. 80 (2018) 326–330, https://doi.org/10.1016/j.yebeh.2017.11.008.
[5] K.C. Rossi, et al., Insufficient sleep, electroencephalogram activation, and seizure risk: Re-evaluating the evidence, Ann. Neurol. 87 (6) (2020) 798–806, https://doi.org/10.1002/ana.25710.
[6] K.L. Dell, et al., Seizure likelihood varies with day-to-day variations in sleep duration in patients with refractory focal epilepsy: a longitudinal electroencephalography investigation, EClinicalMedicine 37 (2021) 100934, https://doi.org/10.1016/j.eclinm.2021.100934.
[7] P. Sudbrack-Oliveira, et al., Sleep architecture in adults with epilepsy: a systematic review, Sleep Med. 53 (2019) 22–27, https://doi.org/10.1016/j.sleep.2018.09.004.
[8] M.C. Ng, M.T. Bianchi, Sleep misperception in persons with epilepsy, Epilepsy Behav. 36 (2014) 9–11, https://doi.org/10.1016/j.yebeh.2014.04.007.
[9] S.H. Wei, W.T. Lee, Comorbidity of childhood epilepsy, J. Formos. Med. Assoc. 114 (11) (2015) 1031–1038, https://doi.org/10.1016/j.jfma.2015.07.015.
[10] B.A. Malow, R.J. Bowes, X. Lin, Predictors of sleepiness in epilepsy patients, Sleep 20 (12) (1997) 1105–1110, https://doi.org/10.1093/sleep/20.12.1105.
[11] S.V. Jain, S.V. Kothare, Sleep and epilepsy, Semin. Pediatr. Neurol. 22 (2) (2015) 86–92, https://doi.org/10.1016/j.spen.2015.03.005.
[12] M. Steriade, F. Amzica, Slow sleep oscillation, rhythmic K-complexes, and their paroxysmal developments, J. Sleep Res. 7 (Suppl 1) (1998) 30–35, https://doi.org/10.1046/j.1365-2869.7.s1.4.x.
[13] W.C. Yeh, et al., Rapid eye movement sleep reduction in patients with epilepsy: a systematic review and meta-analysis, Seizure 96 (2022) 46–58, https://doi.org/10.1016/j.seizure.2022.01.014.
[14] E.H. Smith, et al., Human interictal epileptiform discharges are bidirectional traveling waves echoing ictal discharges, Elife 11 (2022), https://doi.org/10.7554/eLife.73541.
[15] M. Ng, M. Pavlova, Why Are Seizures Rare in Rapid Eye Movement Sleep? Review of the Frequency of Seizures in Different Sleep Stages, vol. 2013, Epilepsy Res Treat, 2013 932790, https://doi.org/10.1155/2013/932790.
[16] O.I. Khan, et al., Interictal spikes in developing rats cause long-standing cognitive deficits, Neurobiol. Dis. 39 (3) (2010) 362–371, https://doi.org/10.1016/j.nbd.2010.05.002.
[17] J.N. Gelinas, et al., Interictal epileptiform discharges induce hippocampal-cortical coupling in temporal lobe epilepsy, Nat. Med. 22 (6) (2016) 641–648, https://doi.org/10.1038/nm.4084.
[18] N.A. Papalambros, et al., Acoustic enhancement of sleep slow oscillations and concomitant memory improvement in older adults, Front. Hum. Neurosci. 11 (2017) 109, https://doi.org/10.3389/fnhum.2017.00109.
[19] A.A. Baril, et al., Slow-wave sleep and MRI markers of brain aging in a community-based sample, Neurology 96 (10) (2021) e1462–e1469, https://doi.org/10.1212/WNL.0000000000011377.
[20] I.E. Scheffer, et al., ILAE classification of the epilepsies: position paper of the ILAE commission for classification and Terminology, Epilepsia 58 (4) (2017) 512–521, https://doi.org/10.1111/epi.13709.
[21] C. Iber, et al., The American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications 2.3, American Academy of Sleep Medicine, Westchester IL, 2016.
[22] S. Roshan, et al., Sleep abnormalities in juvenile myoclonic epilepsy-A sleep questionnaire and polysomnography based study, Seizure 50 (2017) 194–201, https://doi.org/10.1016/j.seizure.2017.06.021.
[23] W. Dement, N. Kleitman, Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming, Electroencephalogr. Clin. Neurophysiol. 9 (4) (1957) 673–690, https://doi.org/10.1016/0013-4694(57)90088-3.
[24] A.A. Winsor, et al., Sleep disruption in children and adolescents with epilepsy: a systematic review and meta-analysis, Sleep Med. Rev. 57 (2021) 101416, https://doi.org/10.1016/j.smrv.2021.101416.
[25] L. Parrino, et al., Distinctive polysomnographic traits in nocturnal frontal lobe epilepsy, Epilepsia 53 (7) (2012) 1178–1184, https://doi.org/10.1111/j.1528-1167.2012.03502.x.
[26] L. Nobili, et al., Nocturnal frontal lobe epilepsy: intracerebral recordings of paroxysmal motor attacks with increasing complexity, Sleep 26 (7) (2003) 883–886.
[27] A. Bonakis, M. Koutroumanidis, Epileptic discharges and phasic sleep phenomena in patients with juvenile myoclonic epilepsy, Epilepsia 50 (11) (2009) 2434–2445, https://doi.org/10.1111/j.1528-1167.2009.02110.x.
[28] E. Arhan, et al., How do children with drug-resistant epilepsy sleep? A clinical and video-PSG study, Epilepsy Behav. 114 (Pt A) (2021) 107320, https://doi.org/10.1016/j.yebeh.2020.107320.
[29] A.M. Pereira, et al., Sleep instability and cognitive status in drug-resistant epilepsies, Sleep Med. 13 (5) (2012) 536–541, https://doi.org/10.1016/j.sleep.2011.12.015.
[30] M.L. Marzec, L.M. Selwa, B.A. Malow, Analysis of the first night effect and sleep parameters in medically refractory epilepsy patients, Sleep Med. 6 (3) (2005) 277–280, https://doi.org/10.1016/j.sleep.2005.01.002.
[31] M. Amiri, B. Frauscher, J. Gotman, Phase-amplitude coupling is elevated in deep sleep and in the onset zone of focal epileptic seizures, Front. Hum. Neurosci. 10 (2016) 387, https://doi.org/10.3389/fnhum.2016.00387.
[32] E. Aanestad, N.E. Gilhus, J. Brogger, Interictal epileptiform discharges vary across age groups, Clin. Neurophysiol. 131 (1) (2020) 25–33, https://doi.org/10.1016/j.clinph.2019.09.017.
[33] C. Beilman, et al., Polysomnography shows sleep fragmentation in patients with inactive inflammatory bowel disease, Ann. Gastroenterol. 33 (6) (2020) 638–644, https://doi.org/10.20524/aog.2020.0529.
[34] J.A. Bigalke, et al., Blunted heart rate recovery to spontaneous nocturnal arousals in short-sleeping adults, Am. J. Physiol. Heart Circ. Physiol. 321 (3) (2021) H558–h566, https://doi.org/10.1152/ajpheart.00329.2021.
[35] N. Barot, M. Nei, Autonomic aspects of sudden unexpected death in epilepsy (SUDEP), Clin. Auton. Res. 29 (2) (2019) 151–160, https://doi.org/10.1007/s10286-018-0576-1, 10.1007/s10286-018-0576-1.
[36] E. Akyüz, et al., Cardiorespiratory findings in epilepsy: a recent review on outcomes and pathophysiology, J. Neurosci. Res. 99 (9) (2021) 2059–2073, https://doi.org/10.1002/jnr.24861.
[37] O. Devinsky, Effects of seizures on autonomic and cardiovascular function, Epilepsy Curr. 4 (2) (2004) 43–46, https://doi.org/10.1111/j.1535-7597.2004.42001.x.
[38] P. Gloor, R.G. Fariello, Generalized epilepsy: some of its cellular mechanisms differ from those of focal epilepsy, Trends Neurosci. 11 (2) (1988) 63–68, https://doi.org/10.1016/0166-2236(88)90166-x.
[39] M. Sammaritano, G.L. Gigli, J. Gotman, Interictal spiking during wakefulness and sleep and the localization of foci in temporal lobe epilepsy, Neurology 41 (2) (1991) 290–297, https://doi.org/10.1212/wnl.41.2_part_1.290. Pt 1.
[40] A. Malow, R.J. Bowes, D. Ross, Relationship of temporal lobe seizures to sleep and arousal: a combined scalp-intracranial electrode study, Sleep 23 (2) (2000) 231–234.

[41] Z. Lin, Q. Si, Z. Xiaoyi, Obstructive sleep apnoea in patients with epilepsy: a meta-analysis, Sleep Breath. 21 (2) (2017) 263–270, https://doi.org/10.1007/s11325-016-1391-3.
[42] P. Hollinger, et al., Epilepsy and obstructive sleep apnea, Eur. Neurol. 55 (2) (2006) 74–79, https://doi.org/10.1159/000092306.
[43] N. Foldvary-Schaefer, et al., Sleep apnea and epilepsy: who's at risk? Epilepsy Behav. 25 (3) (2012) 363–367, https://doi.org/10.1016/j.yebeh.2012.08.032.
[44] N. Nenadic-Baranasic, et al., Overnight video-polysomnographic studies in children with intractable epileptic encephalopathies, Med. Sci. Monit. 24 (2018) 5405–5411, https://doi.org/10.12659/MSM.908911.
[45] M.K. Scullin, Do older adults need sleep? A review of neuroimaging, sleep, and aging studies, Curr. Sleep Med. Rep. 3 (3) (2017) 204–214, https://doi.org/10.1007/s40675-017-0086-z.
[46] R.P. Gelber, et al., Associations of brain lesions at autopsy with polysomnography features before death, Neurology 84 (3) (2015) 296–303, https://doi.org/10.1212/WNL.0000000000001163.
[47] C.Y. Tsai, et al., Associations among sleep-disordered breathing, arousal response, and risk of mild cognitive impairment in a northern Taiwan population, J. Clin. Sleep Med. 18 (4) (2022) 1003–1012, https://doi.org/10.5664/jcsm.9786.
[48] V. Latreille, et al., Neuropsychological correlates of obstructive sleep apnea severity in patients with epilepsy, Epileptic Disord. 21 (1) (2019) 78–86, https://doi.org/10.1684/epd.2019.1029.
[49] M.M. Ohayon, et al., Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan, Sleep 27 (7) (2004) 1255–1273, https://doi.org/10.1093/sleep/27.7.1255.
[50] N.K. Sethi, The relationship between epilepsy, obstructive sleep apnea, and treatment outcome, Sleep Med. Clin. 17 (4) (2022) 639–645, https://doi.org/10.1016/j.jsmc.2022.07.012.
[51] B.A. Malow, et al., Obstructive sleep apnea is common in medically refractory epilepsy patients, Neurology 55 (7) (2000) 1002–1007, https://doi.org/10.1212/wnl.55.7.1002.
[52] Memon, J. and S.N. Manganaro, Obstructive sleep-disordered breathing, in StatPearls. 2023, StatPearls Publishing LLC.: Treasure Island (FL) ineligible companies. Disclosure: Susan Manganaro declares no relevant financial relationships with ineligible companies.
[53] S. Miano, et al., The cooccurrence of interictal discharges and seizures in pediatric sleep-disordered breathing, Epilepsy Behav. 29 (3) (2013) 508–512, https://doi.org/10.1016/j.yebeh.2013.09.002.
[54] L. Giuliano, et al., Parasomnias, sleep-related movement disorders and physiological sleep variants in focal epilepsy: a polysomnographic study, Seizure 81 (2020) 84–90, https://doi.org/10.1016/j.seizure.2020.07.026.
[55] M. Saad, et al., Sleep architecture in patients with idiopathic epilepsy 3 (1) (2019) 33–38.
[56] S. Ancoli-Israel, et al., Periodic limb movements in sleep in community-dwelling elderly, Sleep 14 (6) (1991) 496–500, https://doi.org/10.1093/sleep/14.6.496.
[57] F.X. Hardy De Buisseret, et al., While isolated periodic limb movement disorder significantly impacts sleep depth and efficiency, Co-morbid restless leg syndrome mainly exacerbates perceived sleep quality, Eur. Neurol. 77 (5–6) (2017) 272–280, https://doi.org/10.1159/000471920.
[58] W. Moraes, et al., Effects of aging on sleep structure throughout adulthood: a population-based study, Sleep Med. 15 (4) (2014) 401–409, https://doi.org/10.1016/j.sleep.2013.11.791.
[59] U. Voderholzer, et al., Are there gender differences in objective and subjective sleep measures? A study of insomniacs and healthy controls, Depress. Anxiety 17 (3) (2003) 162–172, https://doi.org/10.1002/da.10101.
[60] C. Liguori, M. Toledo, S. Kothare, Effects of anti-seizure medications on sleep architecture and daytime sleepiness in patients with epilepsy: a literature review, Sleep Med. Rev. 60 (2021) 101559, https://doi.org/10.1016/j.smrv.2021.101559.
[61] B. Legros, C.W. Bazil, Effects of antiepileptic drugs on sleep architecture: a pilot study, Sleep Med. 4 (1) (2003) 51–55, https://doi.org/10.1016/s1389-9457(02)00217-4.