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# Gender differences in prevalence and risk factors of sleep disturbances in patients with epilepsy

Yingfeng Xiao<sup>1,2</sup>, Junying Zhou<sup>3</sup>, Weixi Xiong<sup>1</sup>, Lu Lu<sup>1</sup> and Dong Zhou<sup>1\*</sup>

## Abstract

**Background:** Sleep disturbances are frequently observed in patients with epilepsy (PWE), with adversely effects on life quality and seizure control. The study aimed to assess the gender differences in incidence and factors of sleep disturbances in PWE.

**Methods:** PWE confirmed the diagnosis of epilepsy were consecutively enrolled in this cross-sectional study, with detailed information recorded. A group of healthy participants were recruited as the control. Sleep and mood disorders were evaluated with the Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

**Results:** One hundred and thirty-three patients (age:  $30.2 \pm 10.6$  years, men: 51%) and 150 healthy subjects were recruited in this study. Compared with healthy controls, PWE had higher mean scores of the ISI and BDI ( $p < 0.001$  and  $p = 0.01$ ). There were no significant gender differences in the prevalence and scores of sleep disturbances in PWE. In the overall PWE, nocturnal seizures and focal epilepsy were respectively related to insomnia and poor sleep quality (OR = 3.35,  $p = 0.024$ ; OR = 3.08,  $p = 0.013$ ), and mood disorders were also important factors in sleep disturbances ( $p < 0.05$ ). In the analysis by gender, depression, anxiety, nocturnal seizures and focal epilepsy were associated with insomnia and poor sleep quality in men. For women, however, depression mood was the only factor of sleep disturbances.

**Conclusions:** Though no gender difference was observed in the incidence of sleep disturbances, factors contributing to insomnia and sleep quality were different by gender. The factors and gender differences of sleep disturbances should be taken into account in the clinical treatment.

**Keywords:** Epilepsy, Gender, Sleep disturbances, Insomnia, Sleep quality

## Background

Sleep disturbances are commonly observed in patients with epilepsy (PWE), with a complex interplay underlying [1–4]. Previous studies revealed higher incidences of sleep disturbances in PWE than in healthy controls, with adversely influences on life quality and seizure control

[2, 5–7]. Contributing factors to sleep disturbances in PWE are not thoroughly clarified. Mood disorders, epilepsy-related factors and demographic factors might be involved in the occurrence of sleep disturbances though diverse results existing in prior studies [5, 8–12].

As an important demographic factor, gender differences in sleep have been widely reported [13–15]. Women showed shorter sleep duration, more sleep symptoms, higher prevalence of insomnia and lower rates of sleep apnea than men in the general population [13]. For patients with epilepsy, however, whether gender acts as a

\*Correspondence: zhoudong66@yahoo.de

<sup>1</sup> Department of Neurology, West China Hospital of Sichuan University,

Chengdu 610041, Sichuan, China

Full list of author information is available at the end of the article



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related factor of sleep disturbances was discordant in the limited existing studies [9, 16–18]. Besides, the potential gender differences in the factors of sleep disturbances in PWE have not been systematically studied.

Hence, the study was performed to assess 1) the prevalence and severity of sleep disturbances in patients with epilepsy, 2) whether the sleep disturbances differ between men and women in PWE, 3) the contributing factors of sleep disturbances in each gender group with epilepsy.

## Methods

### Subjects

This cross-sectional study consecutively recruited patients from the Epilepsy Center of West China Hospital between September 2017 and February 2018. Patients older than 16 years of age and confirmed the diagnosis of epilepsy were included. Participants with cognitive deficits or serious medical conditions were excluded for the difficulty in completing the procedures. As for the control group, age- and sex-matched subjects free from epilepsy were enrolled from the general population.

We collected the following clinical data for each patient: demographics (age, gender, body mass index [BMI]); characteristics of epilepsy (age at seizure onset, epilepsy duration, seizure types, seizure frequency, nocturnal seizures, antiepileptic drugs [AEDs]); comorbid medical disorders and other medications besides AEDs. To be more systematically, seizure frequency was classified into three grades (seizure free for at least one year, less than one seizure per month, at least one seizure per month). The study was approved by the Ethics Committee of the West China Hospital, Sichuan University. Informed consents were obtained from all participants.

### Assessments

The Insomnia Severity Index (ISI) is a self-report instrument for recognizing insomnia and grading the severity, which contains seven items on a 5-point scale from 0 to 4 [19]. Patients were instructed to respond according to symptoms and feelings within the previous month. Scores of ISI are categorized in the following manner: 0 to 7, no clinically significant insomnia; 8 to 14, subthreshold insomnia; 15 to 21, moderate clinical insomnia; 22 to 28, severe clinical insomnia. The Pittsburgh Sleep Quality Index (PSQI) is a self-assessment questionnaire evaluating sleep quality and disturbances [20]. The inventory consists of 19 items and measures seven components (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction) over the last month. A global PSQI score higher than 5 was identified as poor sleep quality. Validated and reliable Chinese

version of ISI and PSQI were employed in the present study [21, 22].

Beck Depression Inventory (BDI) is one of the most frequently used self-report rating inventory that measures the severity of depression symptoms [23]. Subjects need to rate 21 items on a scale from 0 to 3 according to their feelings over the last week. The global score ranges from 0 to 63, with higher scores indicating more severe depression symptoms. Beck Anxiety Inventory (BAI) is a 21-question self-report inventory which is used for assessing the severity of anxiety during the past week [24]. Each item is rated on a 4-point scale ranging from 1 (not at all) to 4 (severely), and higher total scores indicate higher levels of anxiety. The Chinese versions of the BDI and BAI have previously been validated and used locally [25, 26].

### Statistical analysis

Data analyses were conducted with IBM SPSS Statistics Software (version 20.0, SPSS, Inc., an IBM company, Chicago, IL, USA). Continuous variables were presented as mean (standard deviation), and categorical variables were shown with counts (%). Independent-sample t-test, the chi-square test and Mann-Whitney U test were used to access the differences in continuous or categorical variables between two groups. Logistic regression analysis was performed to separately evaluate the factors of sleep disturbances in all participants and each gender group. Correction for multiple comparisons was not performed. The null hypothesis was rejected at a  $p$ -value < 0.05.

## Results

### Comparisons between PWE and the control group

A total of 133 patients with epilepsy completed the study procedures and 150 healthy subjects were recruited as controls. Comparisons were conducted between PWE and the healthy control group separately in men, women and the whole sample as shown in Table 1.

Compared with controls, epilepsy patients showed a similar age and higher BMI. In each comparison, the mean score of ISI was significantly higher in PWE than in the control group ( $7.6 \pm 5.8$  vs.  $4.2 \pm 2.6$ ,  $p < 0.001$ ). Moreover, PWE had a significantly higher score of BDI than controls in total group and women ( $p = 0.010$  and  $p = 0.034$ , respectively). However, no significant differences were found in the score of PSQI and BAI between PWE and controls.

### Characteristics in PWE and comparisons by gender

The detail demographic and clinical characteristics of PWE were summarized in Table 2. The patients were consisted of 68 (51%) men and 65 (49%) women. Women showed longer epilepsy duration than men:  $10.4 \pm 7.6$

**Table 1** Comparisons of demographic variables and scale scores by gender in patients with epilepsy and the healthy controls

	Total		P value	Men		P value	Women		P value
	Epilepsy (N = 133)	Control (N = 150)		Epilepsy (n = 68)	Control (n = 75)		Epilepsy (n = 65)	Control (n = 75)	
Age(y)	30.2 ± 10.6	31.9 ± 8.5	0.158	29.5 ± 10.7	30.9 ± 8.5	0.397	31.0 ± 10.6	32.9 ± 8.5	0.253
BMI (kg/m <sup>2</sup> )	22.0 ± 3.2	20.3 ± 2.6	<0.001	22.7 ± 3.4	21.0 ± 2.8	0.001	21.2 ± 2.9	19.6 ± 2.2	<0.001
ISI	7.6 ± 5.8	4.2 ± 2.6	<0.001	7.5 ± 5.7	4.9 ± 2.5	0.042	7.8 ± 6.0	3.5 ± 2.5	<0.001
PSQI	5.2 ± 3.0	5.0 ± 1.8	0.785	4.9 ± 2.7	5.0 ± 1.8	0.309	5.6 ± 3.2	4.9 ± 1.9	0.519
BDI	10.5 ± 8.9	7.4 ± 5.3	0.010	10.7 ± 9.8	7.5 ± 5.6	0.149	10.2 ± 8.0	7.3 ± 5.0	0.034
BAI	30.2 ± 8.5	30.2 ± 6.2	0.261	29.8 ± 8.9	28.5 ± 5.4	0.787	30.6 ± 8.1	32.0 ± 6.5	0.079

Data are presented as counts (%) or mean ± SD

The p-Values are obtained from independent-sample t-test and Mann-Whitney U test

BMI body mass index, ISI Insomnia Severity Index, PSQI Pittsburgh Sleep Quality Index, BDI Beck Depression Inventory, BAI The Beck Anxiety Inventory

**Table 2** Comparisons of demographic and clinical characteristics by gender in patients with epilepsy (n = 133)

	Total (n = 133)	Men (n = 68)	Women (n = 65)	p
Age (y)	30.2 ± 10.6	29.5 ± 10.7	31.0 ± 10.6	0.399
BMI (kg/m <sup>2</sup> )	22.0 ± 3.2	22.7 ± 3.4	21.2 ± 2.9	0.007
Age at seizure onset (y)	21.2 ± 11.8	21.7 ± 12.0	20.8 ± 11.7	0.644
Epilepsy duration (y)	9.0 ± 7.5	7.8 ± 7.2	10.4 ± 7.6	0.043
Nocturnal seizures (n, %)	40 (30.1)	20 (29.4)	20 (30.8)	0.865
Seizure types (n, %)				0.035
Focal	82 (61.7)	36 (52.9)	46 (70.8)	
General	51 (38.3)	32 (47.1)	19 (29.2)	
AEDs (n, %)				0.902
Drug free	20 (15.2)	11 (16.4)	9 (13.8)	
AED monotherapy	47 (35.6)	24 (35.8)	23 (35.4)	
AED polytherapy	65 (49.2)	32 (47.8)	33 (50.8)	
Seizure frequency (n, %)				0.415
Seizure free	29 (21.8)	17 (25.0)	12 (18.5)	
< 1 seizure/m	40 (30.1)	22 (32.4)	18 (27.7)	
≥ 1 seizure/m	64 (48.1)	29 (42.6)	35 (53.8)	
ISI	7.6 ± 5.8	7.5 ± 5.7	7.8 ± 6.0	0.772
Moderate to severe clinical insomnia (ISI > 14)	27 (20.5)	14 (20.6)	13 (20.3)	0.969
PSQI	5.2 ± 3.0	4.9 ± 2.7	5.6 ± 3.2	0.256
Poor sleep quality (PSQI > 5)	53 (40.2)	24 (35.3)	29 (45.3)	0.241
BDI	10.5 ± 8.9	10.7 ± 9.8	10.2 ± 8.0	0.778
BAI	30.2 ± 8.5	29.8 ± 8.9	30.6 ± 8.1	0.292

Data are presented as counts (%) or mean ± SD

The p-values are obtained from independent-sample t-test, the chi-square test and Mann-Whitney U test

BMI body mass index, AED antiepileptic drug, ISI Insomnia Severity Index, PSQI Pittsburgh Sleep Quality Index, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory

vs.  $7.8 \pm 7.2$  years ( $p = 0.043$ ). Significant difference was observed in seizure types in women and men ( $p = 0.035$ ). No remarkable differences were found in age, age at seizure onset, nocturnal seizures, use of antiepileptic drugs and seizure frequency between gender groups.

ISI scores indicated that 40.9% of PWE were under at least subthreshold insomnia ( $ISI > 7$ ), and 20.5% of patients suffered from moderate to severe clinical insomnia ( $ISI > 14$ ) which was similar in both gender groups (20.6% in males and 20.3% in females). Fifty-three (40.2%) patients were “poor sleepers” with the PQSI score

higher than five (35.3% in males and 45.3% in females). Overall, differences were not significant in the prevalence of insomnia and poor sleep quality between men and women with epilepsy, so did the mean scores of the scales, which revealing the severity of sleep disturbances and mood disorders.

**Factors related to insomnia and sleep quality in PWE**

According to the logistic regression analysis, in the whole group, clinical insomnia (ISI > 14) was significantly associated with nocturnal seizures ( $p=0.024$ ), BDI scores ( $p=0.019$ ) and BAI scores ( $p=0.017$ ) as shown in Table 3. Poor sleep quality (PSQI > 5) was associated with BDI scores ( $p<0.001$ ) and focal epilepsy ( $p=0.013$ ).

When furtherly analyzing in gender groups, insomnia was associated with higher BAI scores ( $p=0.002$ ) and nocturnal seizures ( $p=0.036$ ) in men with epilepsy. Poor sleep quality was related to BDI scores ( $p=0.004$ ) and focal epilepsy ( $p=0.044$ ) However, both insomnia and sleep quality were solely related to higher BDI scores ( $p=0.008$  and  $p=0.002$ , respectively) in women with epilepsy.

**Discussion**

**Prevalence of sleep disturbances in PWE and comparisons by gender**

In the present study, the prevalence of clinical insomnia in epilepsy patients was 20.5% as compared with 15% of the Chinese general population, and within the range of 14.5-51% among PWE in other prior studies [5, 9, 16, 17, 27]. In addition, 40.2% of PWE were “poor sleepers” in this study, with 39-72% in earlier literatures [9, 17, 28]. The prevalence rates vary in the researches, in some extent it may due to different assessment measures and inclusion criteria designed for diverse research objectives.

It was reported that women were more likely to have trouble in sleep than men in the general population [13]. For patients with epilepsy, controversy about gender differences in sleep persisted and limited studies focused on the field. No significant gender difference was found regarding to the prevalence and severity of sleep disturbances measured by validated scales in this study, which was consistent with some prior studies [9, 29, 30]. However, a few studies suggested that women with epilepsy were vulnerable to have sleep disturbances compared with men just like the general population [17, 18].

**Related factors of sleep disturbances in the overall group**

Mood disorders were often observed in patients with epilepsy and considered to be strongly associated with sleep disturbances in most related reports [9, 10, 16]. In the present study, depression mood was the common factor of both insomnia and poor sleep quality, whereas anxiety was merely related to insomnia. The results were in line with prior studies that mood disorders indeed play an important role in sleep disturbances.

Except for mood disorders, epilepsy-related factors were associated with sleep disturbances. Nocturnal seizure and focal epilepsy were respectively correlated with insomnia and poor sleep quality in the study. Previous reports had showed that nocturnal seizure was more frequent in epilepsy patients suffering from insomnia, with detrimental effects on sleep quality, daytime sleepiness and rapid eye movement sleep [12, 31, 32]. As to the influence of seizure types, the outcome was in agreement with some prior researches which also revealed varying sleep problems resulted from different types of seizures [33, 34].

Apart from nocturnal seizure and seizure types, no other epilepsy-related factors were found contributing to insomnia and sleep quality in present study. However,

**Table 3** Factors associated with sleep disturbances in patients with epilepsy

	Total (n = 133)			Men (n = 68)			Women (n = 65)		
	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value
<b>Insomnia</b>									
Nocturnal seizures	3.35	1.17-9.60	0.024	5.55	1.12-27.61	0.036	-	-	-
BDI scores	1.07	1.01-1.14	0.019	-	-	-	1.12	1.03-1.21	0.008
BAI scores	1.08	1.01-1.15	0.017	1.15	1.05-1.26	0.002	-	-	-
<b>Sleep quality</b>									
Focal epilepsy	3.08	1.27-7.48	0.013	3.49	1.04-11.79	0.044	-	-	-
BDI scores	1.14	1.07-1.21	<0.001	1.11	1.03-1.19	0.004	1.19	1.07-1.32	0.002

The p-values are obtained from logistic regression analysis

OR odds ratio, CI Confidence Interval, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory

prior studies reported the relationships of sleep disturbances and other epilepsy-related factors, such as the number of AEDs and seizure control [5, 17]. Further researches are required to reach a consensus.

#### Related factors of sleep disturbances in gender groups

No study had analyzed the potential gender differences in the factors of sleep disturbances in PWE. This study furtherly conducted analysis on the factors associated with sleep disturbances by gender. Though epidemiological results did not display any gender difference in the incidence of sleep disturbances, logistic regression analysis indicated that the factors in different gender groups were not identical.

Depression, anxiety and epilepsy-related factors of nocturnal seizure and focal epilepsy were important factors of sleep disturbances in men with epilepsy. However, the study didn't find any epilepsy-related factors associated with sleep disturbances in women. Depression was the solely factor related to sleep in women with epilepsy.

The gender difference in sleep disturbances was difficult to have a clear explanation. It might be ascribed to the disparate social roles and expectations of each gender, as well as the multiple and complex interactions of neuronal and humoral.

Anticipated to undertake most financial support for family, to handle work well and develop kinds of social activities, men always confront relatively more complicated and stressful social relationships than women, who spend more time caring families [35, 36]. It can be inferred that living with epilepsy increase trouble and confusion in different aspects for men and women confronted with different stress and responsibilities [37, 38]. Moreover, gender differences on circadian seizure distribution and susceptibility to epileptic seizures were illustrated before, and steroid hormone was considered important actor in the process [39, 40].

With complicated relationships in sleep, endocrine system, social participations and epilepsy existing in varying outcomes between two gender groups, further researches are recommended to explore the exact mechanism underlying.

#### Limitations

There are several limitations in our study. First, potential sample selection bias might arise because patients in our study were recruited from a tertiary epilepsy center, in which patients tend to suffer more from epilepsy. Second, as this study was a cross-sectional design, we cannot identify the cause-and-effect relationship between epilepsy related factors and sleep disturbances. Future

studies with longitudinal follow-ups and comparisons are required. Furthermore, information on sleep disturbances we can get was limited only with scales. It would be much more credible if objective measures such as polysomnography and actigraphy be applied to the research.

#### Conclusions

In short, no difference was found in the incidence of sleep disturbances between men and women with epilepsy. However, gender differences existed in the factors associated with insomnia and sleep quality. Nocturnal seizures, focal epilepsy, depression and anxiety acted important roles in men, while only depression was the factor of insomnia and sleep quality in women. Hence when it comes to clinical diagnosis and treatment of sleep disturbances in patients with epilepsy, gender differences should be taken into account.

#### Abbreviations

PWE: Patients with epilepsy; ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; AEDs: Antiepileptic drugs.

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#### Authors' contributions

Yingfeng Xiao is the first author of this manuscript, and she participated in data collection, patients' follow-up, drafting and revising the paper. Junying Zhou participated in study designing and data analysis. Weixi Xiong and Lu Lu have made great assistants in data collection. Professor Dong Zhou have made great contribution to study designing, and he is the Corresponding author. All authors read and approved the final manuscript.

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#### Availability of data and materials

Data may be available from the authors on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

The study was approved by the Ethics Committee of the West China Hospital, Sichuan University. Informed consents were obtained from all participants.

##### Consent for publication

The consents for publication were obtained from all participants.

##### Competing interests

Author Dong Zhou is the associate editor for *Acta Epileptologica*. Author Dong Zhou was not involved in the journal's review of, or decisions related to this manuscript.

##### Author details

<sup>1</sup>Department of Neurology, West China Hospital of Sichuan University, Chengdu 610041, Sichuan, China. <sup>2</sup>Department of Neurology, The Bishan Hospital of Chongqing, Chongqing 402760, China. <sup>3</sup>Sleep Medicine Center, West China Hospital of Sichuan University, Chengdu 610041, Sichuan, China.

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