

Depression is a major determinant of sleep abnormalities in patients with epilepsy

A depressão é um dos principais determinantes das anormalidades do sono em pacientes com epilepsia

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ABSTRACT

Introduction: We aimed to identify sleep disorders in patients with epilepsy and compare this group with a healthy population. We also analyzed the features of sleep disorders in patients with epilepsy to demonstrate the effect of seizures and seizure types on sleep. **Methods:** Our study assessed 43 patients with epilepsy and 53 age- and gender-matched healthy controls. The demographic and clinical data of all participants were recorded. The Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index (PSQI), International Restless Legs Syndrome Study Group Rating Scale, Berlin Questionnaire, and Beck Depression Inventory (BDI) were administered to all study subjects. The interview used to evaluate insomnia is based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition – DSM-5 diagnostic criteria. **Results:** Twenty-four patients (55.8%) and 26 controls (49.1%) are women. The mean age of patients and controls was 34.2±11.37 (16–71) and 34.6±11.28 (16–77), respectively. Patients with epilepsy had depression more often than controls, a result that was statistically significant ($p<0.0001$). We found no statistically significant difference between sleep parameters of patients and controls with normal BDI scores ($p>0.05$). Patients with depression had worse results on the Berlin Questionnaire and PSQI total score, with statistical significance ($p=0.002$). Nocturnal seizures, seizure type, and drug treatment had no effect on sleep ($p>0.05$). **Conclusion:** We concluded that depression rather than epilepsy negatively affects sleep, suggesting that all patients should be asked about their mood and sleep complaints.

Keywords: Epilepsy; Seizures; Depression; Sleep; Prognosis.

RESUMO

Introdução: O objetivo deste estudo foi identificar distúrbios do sono em pacientes com epilepsia e compará-los com uma população saudável. Também foram examinadas as características dos distúrbios do sono em pacientes com epilepsia para demonstrar o efeito e os tipos de convulsões no sono. **Métodos:** O estudo consistiu em 43 pacientes com epilepsia e 53 controles saudáveis pareados por idade e sexo. Os dados demográficos e clínicos de todos os participantes foram registrados. Todos os participantes do estudo receberam a Escala de Sonolência de Epworth, o Índice de Qualidade do Sono de Pittsburgh (*Pittsburgh Sleep Quality Index* — PSQI), o Questionário do Grupo Internacional de Estudos das Pernas Inquietas, o Questionário de Berlim e o Inventário de Depressão de Beck. A entrevista usada para avaliar a insônia é baseada nos critérios do DSM-V. **Resultados:** Vinte e quatro pacientes (55,8%) são do sexo feminino e vinte e seis do grupo controle (49,1%) são do sexo feminino. A média de idade dos pacientes e do grupo controle é de 34,2±11,37 (16–71) e 34,6±11,28 (16–77), respectivamente. Pacientes com epilepsia sofrem mais de depressão do que os controles e esse resultado é estatisticamente significativo ($p<0,0001$). Não houve diferença estatisticamente significativa entre os parâmetros do sono dos pacientes e dos controles que apresentaram escores de Beck normais ($p>0,05$). Pacientes com depressão apresentam resultados piores no escore total do PSQI de Berlim, o que é estatisticamente significativo ($p=0,002$). As convulsões noturnas, o tipo de convulsão e o tratamento medicamentoso não afetaram o sono ($p>0,05$). **Conclusão:** Determinamos que a depressão, e não a epilepsia, afeta negativamente o sono dos pacientes, sugerindo que todos os pacientes devem ser questionados sobre seu humor e queixas de sono.

Palavras-chave: Epilepsia; Convulsões; Depressão; Sono; Prognóstico.

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INTRODUCTION

Epilepsy is a common neurological disease with a prevalence of 0.4–1%. Sleep is an important aspect of life in patients with epilepsy, as they have a higher propensity for sleep disorders than the general population¹. Epilepsy and sleep mutually affect each other. Both diurnal and nocturnal seizures deteriorate sleep structure¹. Sleep apnea and sleep deprivation are among the most common sleep disorders that directly impact sleep quality and thereby trigger seizures². Insomnia is one of the most frequent sleep disorders in patients with epilepsy, influencing their mood negatively^{3,4}. Excessive daytime sleepiness, poor sleep quality, and restless legs syndrome are more common in patients with epilepsy and worsen their quality of life⁵. Mood disorders, particularly depression, are known to have a higher prevalence in patients with epilepsy than the general population, which also has a negative effect on sleep^{6,7,8}.

We aimed to identify sleep disorders in patients with epilepsy and compare this group with a healthy population. We also analyzed the features of sleep disorders in patients with epilepsy to demonstrate the effect of nocturnal seizures and seizure types on sleep.

METHODS

Our study assessed 43 patients with epilepsy, treated at the Epilepsy Outpatient Clinic of Istanbul University, Istanbul School of Medicine, Department of Neurology. The patients were recruited consecutively and selected according to the following criteria: being over 18 years of age, literate, without intellectual disability. We excluded patients with epilepsy who had comorbid chronic diseases and were taking medications other than antiepileptic drugs (AEDs). We also included 53 age-matched healthy controls. Demographic characteristics of both patients and healthy controls were recorded, as well as the clinical features of the patients.

We administered the questionnaires and conducted an interview to determine the presence of sleep disorders and insomnia. The descriptions of our questionnaires are:

Epworth Sleepiness Scale (ESS): ESS is an eight-item questionnaire that evaluates daytime sleepiness. A total score equal to or greater than 10 indicates excessive daytime sleepiness⁹.

International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale: The IRLSSG rating scale is considered the gold standard for evaluating restless legs syndrome (RLS) severity. This rating scale comprises 10 questions, with scores ranging from 0 to 4. The score is classified as 1–10: mild; 11–20: moderate; 21–30: severe; 31–40: very severe¹⁰.

Pittsburgh Sleep Quality Index (PSQI): In PSQI, general sleep patterns are evaluated based on 18 questions

distributed into 7 subscales: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the prior month. A total score of five or more indicates poor sleep quality¹¹.

Berlin Questionnaire (BQ): BQ screens for obstructive sleep apnea (OSA) in the community and comprises 10 questions in 3 categories. Each category is evaluated individually, and if two or more categories have positive results, the OSA risk is considered high¹².

Beck Depression Inventory (BDI) and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition – DSM-5 criteria: These criteria evaluate mood and depression, as well as insomnia^{13,14}.

Test results of both groups were compared, followed by a study of the relationship between clinical findings of epilepsy (seizure type, presence of nocturnal seizures, seizure freedom, and treatment) and test results.

All participants were informed that this research analyzes the features of sleep disorders in patients with epilepsy and the healthy population. Informed written consent was obtained from all participants before they answered the questionnaires.

The study was approved by the Ethics Committee of Istanbul University, Istanbul School of Medicine (2015/1741).

Statistical analysis

Study data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 21.0, and a $p < 0.05$ was considered statistically significant. Continuous variables are expressed as mean \pm standard deviation (SD); categorical variables are presented as frequencies and percentages. The chi-square test, the Student's t-test, and the Neyman-Pearson likelihood ratio were used to determine the statistical significance of differences in means and proportions.

RESULTS

Our study included 43 patients with epilepsy and 53 healthy controls. Twenty-four patients (55.8%) are women, and 19 (44.2%) are men. Twenty-six controls (49.1%) are women, and 27 (50.9%) are men. The mean age of the patients was 34.2 ± 11.37 (16–71) and of the control group was 34.6 ± 11.28 (16–77). We found no significant difference between the two groups as to age, gender, and body mass index (BMI) ($p > 0.05$). The mean age at seizure onset was 19.2 ± 14.93 (1–69). Twenty-three (53.5%) patients had focal seizures, and 20 (46.5%) had generalized seizures (Table 1).

All patients were using AEDs — 22 (51.2%) on monotherapy and 21 (48.8%) on polytherapy. The most frequently used drugs were levetiracetam (11 patients — 11.5%), carbamazepine (5 patients — 5.2%), and lamotrigine

(3 patients — 3.6%). Mood disorders are very likely to affect sleep quality. The prevalence of depression was 37.2% (27 individuals) in the patient group and 16.9% (9 individuals) in the control group, which was statistically significant according to BDI ($p < 0.001$) (Table 1).

Table 1. Demographic and clinical features of patient and control groups.

	n=43 (%)	Control=53 (%)	p-value
Age (years)	34.2±11.37 (16–71)	34.6±11.28 (16–77)	0.85
Gender (Female/ Male)	24 (55.8)/19 (44.2)	26 (49.1)/27 (50.9)	0.51
Age onset of seizures (year)	19.2±14.93	-	
Duration of disease (year)	15.0±12.88 (1–48)	-	
Epilepsy type			
Focal	23 (53.5)	-	
Generalized	20 (46.5)		
Seizure freedom (in the last year)			
Yes	13 (30.2)		
No	30 (69.8)		
Seizure type			
Focal	13 (30.2)		
SGS	10 (23.3)		
GS	20 (46.5)		
Cranial MRI			
Normal	21 (48.8)	-	
Abnormal	22 (51.2)		
EEG			
Normal	9 (20.9)		
Generalized abnormality	19 (44.2)		
Focal abnormality	15 (34.9)	-	
AED			
Monotherapy	22 (51.2)		
CBZ	5 (11.6)		
VPA	2 (4.7)		
LEV	11 (26.6)		
LTG	3 (7)		
OXC	1 (2.3)		
Polytherapy	21 (48.8)		
BMI	25±3.8	24±3.7	0.56
BDI scores	14.9±10.9	6.6±5.3	<0.0001*

* $p < 0.05$; EEG: electroencephalogram; AED: antiepileptic drugs; CBZ: carbamazepine; VPA: valproate; LEV: levetiracetam; LTG: lamotrigine; OXC: oxcarbazepine; BDI: Beck Depression Inventory; BMI: body mass index; SGS: secondary generalized seizure; GS: generalized seizure. MRI: Magnetic resonance imaging.

In order to eliminate the negative impact of depression on sleep and focus only on the impact of epilepsy on sleep, we compared sleep parameters of patients and controls with normal BDI scores. No statistically significant difference was found between the groups ($p > 0.05$) (Table 2).

Epilepsy type, nocturnal seizures, monotherapy/polytherapy, and seizure freedom were not effective sleep parameters ($p > 0.05$) (Table 3).

Duration of disease and age at onset showed no significant correlation to test scores ($p > 0.05$) (Table 4).

We divided our patients with epilepsy according to BDI. Patients with high BDI scores had worse PSQI total score (Table 5).

DISCUSSION

Our main objective was to identify sleep disorders in patients with epilepsy. Our study showed that depression is more common in patients with epilepsy than in healthy controls, as also indicated previously^{15,16}. The higher frequency of depression in patients with epilepsy can be explained as an effect of having a chronic disease¹⁷. On the other hand, depression has a negative effect on sleep^{5,18,19}. We detected no difference between patients and healthy controls with normal BDI scores regarding sleep scores.

Insomnia is highly reported in patients with epilepsy²⁰. Seizures, which cause sleep fragmentation and arousals, and/or the effects of AEDs might justify this high prevalence²¹. Our study found no significant difference in terms of insomnia.

Table 2. Questionnaire scores of the patients and controls with normal Beck Depression Inventory scores.

	Patients n:16 (%)	Controls n: 44 (%)	p-value
ESS			
0–9	16 (100)	40 (90.9)	0.56
>10	0 (0)	4 (9.1)	
IRLSSG rating scale			
0	14 (87.4)	37 (84.1)	0.93
1–10	1 (6.3)	4 (9.1)	
11–20	1 (6.3)	3 (6.8)	
Berlin Questionnaire			
0–1	14 (87.5)	40 (90.9)	0.65
>2	2 (12.5)	4 (9.1)	
PSQI			
0–4	13 (81.2)	34 (77.3)	0.74
>5	3 (18.8)	10 (22.7)	
Insomnia (+/-) (%)	2 (12.5)/14 (87.5)	1 (2.3)/43 (97.7)	0.17

BDI: Beck Depression Inventory; ESS: Epworth Sleepiness Scale. IRLSSG: International Restless Legs Syndrome Study Group; PSQI: Pittsburgh Sleep Quality Index.

Table 3. Sleep questionnaire results of patients with epilepsy and normal Beck Depression Inventory scores.

n=16	Epilepsy type (Focal/Generalized) (n/%)	Nocturnal seizure (Yes/No) (n/%)	Treatment Monotherapy/Polytherapy (n/%)	Seizure free (Yes/No) (n/%)
ESS				
0-9	5 (100)/11 (100)	7 (100)/9 (100)	8 (100)/8 (100)	6 (100)/10 (100)
>10	0 (0)/0 (0)	0 (0)/0 (0)	0 (0)/0 (0)	0 (0)/0 (0)
IRLSSG rating scale				
0	5 (100)/9 (81.8)	6 (85.7)/8 (88.9)	7 (7.5)/7 (87.5)	6 (100)/8 (80)
1-10	0 (0)/1 (9.1)	0 (0)/1 (11.1)	0 (0)/1 (12.5)	0 (0)/1 (10)
11-20	0 (0)/1 (9.1)	1 (14.3)/0 (0)	1 (12.5)/0 (0)	0 (0)/1 (10)
Berlin Questionnaire				
0-1	5 (100)/9 (81.8)	7 (100)/7 (77.8)	7 (87.5)/7 (87.5)	5 (83.3)/9 (90)
>2	0 (0)/2 (18.2)	0 (0)/2 (22.2)	1 (12.5)/1 (12.5)	1 (16.7)/1 (0)
PSQI				
0-4	4 (80)/9 (81.8)	6 (85.7)/7 (77.8)	8 (100)/5 (62.5)	4 (66.7)/9 (90)
>5	1 (20)/2 (18.2)	1 (14.3)/2 (22.2)	0 (0)/3 (37.5)	2 (33.3)/1 (10)
Insomnia (+) (%)	0 (0)/2 (18.2)	1 (11.1)/1 (14.3)	1 (12.5)/1 (12.5)	1 (10.0)/1 (16.7)

BDI: Beck Depression Inventory; ESS: Epworth Sleepiness Scale. IRLSSG: International Restless Legs Syndrome Study Group; PSQI: Pittsburgh Sleep Quality Index.

Table 4. Sleep questionnaire results of patients with epilepsy and normal Beck Depression Inventory scores.

n=16		ESS	PSQI	IRLSSG rating scale	Berlin Questionnaire
Age at onset	Pearson's correlation	0.16	-0.36	-0.08	0.46
	p-value	0.55	0.17	0.74	0.07
Duration of disease	Pearson's correlation	0.16	-0.05	0.18	0.13
	p-value	0.53	0.84	0.48	0.61

BDI: Beck Depression Inventory; ESS: Epworth Sleepiness Scale; IRLSSG: International Restless Legs Syndrome Study Group; PSQI: Pittsburgh Sleep Quality Index; *p<0.05.

Table 5. Questionnaires of patients with normal and abnormal Beck Depression Inventory scores.

n=43	Normal BDI scores n=16 (%)	Abnormal BDI scores n=27 (%)	p-value
ESS			
0-9	16 (100)	21 (77.8)	0.06
>10	0 (0)	6 (22.2)	
IRLSSG rating scale			
0	14 (87.4)	20 (76.9)	0.27
1-10	1 (6.3)	0 (0)	
11-20	1 (6.3)	3 (11.5)	
21-30	0	3 (11.5)	
Berlin Questionnaire			
0-1	14 (87.5)	22 (81.5)	0.69
>2	2 (12.5)	5 (18.5)	
PSQI			
0-4	13 (81.3)	8 (29.6)	0.002*
>5	3 (18.7)	19 (70.4)	
Insomnia (+) (%)	2 (12.5)	6 (22.2)	0.68

BDI: Beck Depression Inventory; ESS: Epworth Sleepiness Scale. IRLSSG: International Restless Legs Syndrome Study Group; PSQI: Pittsburgh Sleep Quality Index; *p<0.05.

Sleep problems in patients with epilepsy might have several pathophysiological explanations. Firstly, seizures are known to have a worsening effect on sleep. Both diurnal and nocturnal seizures deteriorate sleep structure. In addition, nocturnal seizures decrease total sleep duration, sleep efficiency, and increase sleep fragmentation, latency, and awakening^{1,22}. Postictal state, which is usually caused by nocturnal seizures, decreases sleep quality²³.

We also analyzed the sleep features of patients with epilepsy and without depression according to BDI and found no significant difference as to age at onset, duration of disease, epilepsy type, nocturnal seizures, monotherapy/polytherapy, and seizure freedom. Contradictory arguments have been presented about the effects of epilepsy type on sleep. Some researchers state that patients with focal epilepsy have poorer sleep quality than those with generalized epilepsy, while others report no significant difference^{19,24}. A similar controversy also exists about diurnal/nocturnal seizures, seizure frequency, or seizure freedom in the previous year. Nocturnal seizures are believed to affect sleep by causing arousals and excessive daytime sleepiness^{1,19,25,26}.

The effect of AEDs on sleep has also been a controversial subject among neurologists. Some argue that AEDs worsen sleep problems, leading to especially excessive daytime

sleepiness^{21,27}. Conversely, many researchers declare that the number and type of AEDs do not have any significant effect on sleep^{1,23,28}. A subject that contradictory should be clarified with further detailed studies. We found no statistically significant difference with respect to monotherapy and polytherapy among our patients.

To double-check our starting hypothesis, we compared the sleep scales of patients with normal and high BDI scores. We identified that patients with depression had worse PSQI scores (total score, subjective sleep quality, sleep latency, daytime

dysfunction) than individuals without this condition, confirming that depression has a greater impact on sleep disorders.

Our study has a few limitations. First, the sample size is small. In addition, sleep disorders were evaluated according to tests rather than polysomnography.

Epilepsy is known to have negative effects on sleep. However, comorbid depression may lead to even poorer sleep quality. Therefore, all patients with epilepsy must be asked about their mood and sleep complaints in routine follow-up to ensure the effectiveness of treatment.

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