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The association between epilepsy and sleep disturbance in US adults: the mediating effect of depression

Qianhui Wen[1,2], Qian Wang[1,2] and Hua Yang[1,2*]

Abstract

Background People with epilepsy (PWE) frequently experience sleep disturbances that can severely affect their quality of life. Depression is also a common symptom in the PWE population and can aggravate sleep problems. However, the interplay between epilepsy, depression, and sleep disturbances is not yet fully understood. Our study was designed to investigate the association between epilepsy and sleep disturbances in US adults and to determine whether depressive symptoms play a mediating role in this relationship.

Methods We examined data from the National Health and Nutrition Examination Survey (NHANES) spanning January 1, 2015, to March 2020, before the pandemic.A total of 10,093 participants aged ≥ 20 years with complete data on epilepsy and sleep disturbance were included. Weighted multiple logistic regression and mediation analysis were used to explore the associations among depression, epilepsy, and sleep disturbance. Interaction effects of epilepsy with various covariates were also investigated.

Results Epilepsy was associated with depression and sleep disturbances. Weighted logistic regression analysis revealed a significant association between epilepsy and sleep disturbances (OR = 3.67, 95% CI = 1.68–8.04). Depression partially mediated this relationship, demonstrating a mediation effect of 23.0% (indirect effect = 0.037, $P < 0.001$). Subgroup analyses revealed variations in the relationship between epilepsy and sleep disturbances among different groups. Furthermore, interaction analyses revealed significant interactions between epilepsy and age ($P = 0.049$) and hypertension ($P = 0.045$).

Conclusions Our study utilizing NHANES data confirmed that depression partially mediated the association between epilepsy and sleep disturbance. Additionally, we observed differences in this association across demographic groups. Addressing depressive symptoms in PWE may improve their sleep quality, but further research is needed to explore the underlying mechanisms.

Keywords Epilepsy, Sleep disturbance, Depression, Mediation effect, NHANES

*Correspondence:
Hua Yang
yanghua202203@163.com
[1]Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China
[2]Key Laboratory of Obstetric & Gynecologic and Pediatric Diseases and Birth Defects of Ministry of Education, Sichuan University, Chengdu, Sichuan, China

Introduction

Sleep disturbances frequently present serious challenges for individuals diagnosed with epilepsy. Earlier studies indicate that people with epilepsy (PWE) experience twice the frequency of sleep disturbances compared to their healthy counterparts [1, 2]. These disruptions primarily encompass difficulties in the onset and maintenance of sleep [2], regular nighttime awakenings, and episodes of obstructive sleep apnea [3]. Consequently, PWE often experience fatigue, cognitive impairments, and increased daytime sleepiness, compounding the difficulties they encounter in managing their health [4, 5].

Numerous studies have investigated the possible pathophysiological mechanisms contributing to sleep disturbances in this population. It is widely recognized that multiple contributors may influence the onset and development of sleep disturbances, including alterations in neurotransmitter systems, neuroendocrine dysfunction, and changes in sleep architecture [6]. Additionally, the adverse effects of antiepileptic medications [7], frequent nocturnal seizures [8], poor sleep hygiene habits, and psychological factors may worsen sleep issues in PWE.

Depression frequently coexists with epilepsy, affecting more than one-third of PWE [9]. A study conducted in China reported that 28.8% of PWE suffer from depression [10]. Fiest et al., in a meta-analysis, found that depression rates in PWE are 23.1% [11]. Hospitalized PWE exhibit an even higher depression rate, exceeding 50%, compared to approximately 8% among patients in remission [12]. The combination of social isolation, dysfunction, and inappropriate use of antiepileptic medications has the potential to trigger depressive symptoms [13]. Population-based studies suggest that individuals with prior depression have an elevated likelihood of developing epilepsy, ranging from four to seven times the risk compared to the broader population [14]. The comorbidity of epilepsy and depression is often caused or induced by a combination of pathological mechanisms, such as neurotransmitter imbalance, hippocampal dysfunction, and endocrine dysregulation [15, 16].

Notably, sleep disturbances and symptoms of depression often co-occur and exhibit patterns of interaction and influence [17]. Depressed individuals commonly suffer from a variety of sleep issues, including insomnia, excessive daytime sleepiness, and disrupted sleep-wake patterns [18]. Sleep disturbances can also serve as precipitating factors in the onset and progression of depression, exerting adverse effects on emotional regulation, cognitive function, and neuroendocrine homeostasis.

Although depression and sleep disturbances have been extensively discussed in the context of epilepsy, existing studies often isolate the relationship between epilepsy and sleep or between epilepsy and depression. However, this segmented perspective may overlook the potential complex interactions among these three factors. Understanding these interactions is crucial for enhancing management strategies and improving treatment outcomes. Thus, our study aimed to evaluate the association between epilepsy and sleep disturbances among adults in the United States, specifically investigating the potential role of depression as a mediator.

Methods

Study design and participants

Our study drew on data from the National Health and Nutrition Examination Survey (NHANES), a comprehensive database initiated in 1999, which evaluates the health and nutritional status of the U.S. population [19]. To ensure national representativeness, the NHANES employs a continuous multistage probability sampling method. The NHANES study was granted ethical approval by the Research Ethics Review Board of the National Center for Health Statistics, and all participants provided informed consent prior to their involvement. Furthermore, this database is publicly accessible, and no additional ethical or administrative permissions are required. We adhered to NHANES guidelines and regulations in all analyses conducted. We included participants from the NHANES data collected between January 1, 2015, and March 2020 (prepandemic), as this period encompassed the comprehensive set of variables essential for this investigation, including the utilization of prescription medications, sleep assessment, and the Patient Health Questionnaire 9 (PHQ-9). Figure 1 illustrates the diagram of the screening procedure.

Antiepileptic drug use and epilepsy diagnosis

The NHANES survey assessed participants to determine if they had taken any prescription drugs in the past 30 days, querying them on the generic names of the medications, the primary reasons for their use, and any corresponding ICD-10-CM codes provided. Detailed codes and names of antiepileptic drugs are listed in Table S1. PWE were identified by their use of antiepileptic medications and the relevant ICD-10-CM codes [20, 21].

Assessment of sleep disturbance

Sleep parameter data were obtained from the "Sleep Disorders" dataset of the NHANES questionnaire [22]. Participants reported their typical nightly sleep hours on weekdays or workdays. Sleep duration was categorized as short (<7 h), normal (7–9 h), or long (>9 h) based on these reports [23]. Participants were also asked whether they had informed a doctor about their sleep difficulties, which was used to assess the presence of trouble sleeping. Table 1 outlines the calculation of a sleep quality score, incorporating sleep duration, trouble sleeping, snoring, snorting, or stopping breathing, and excessive

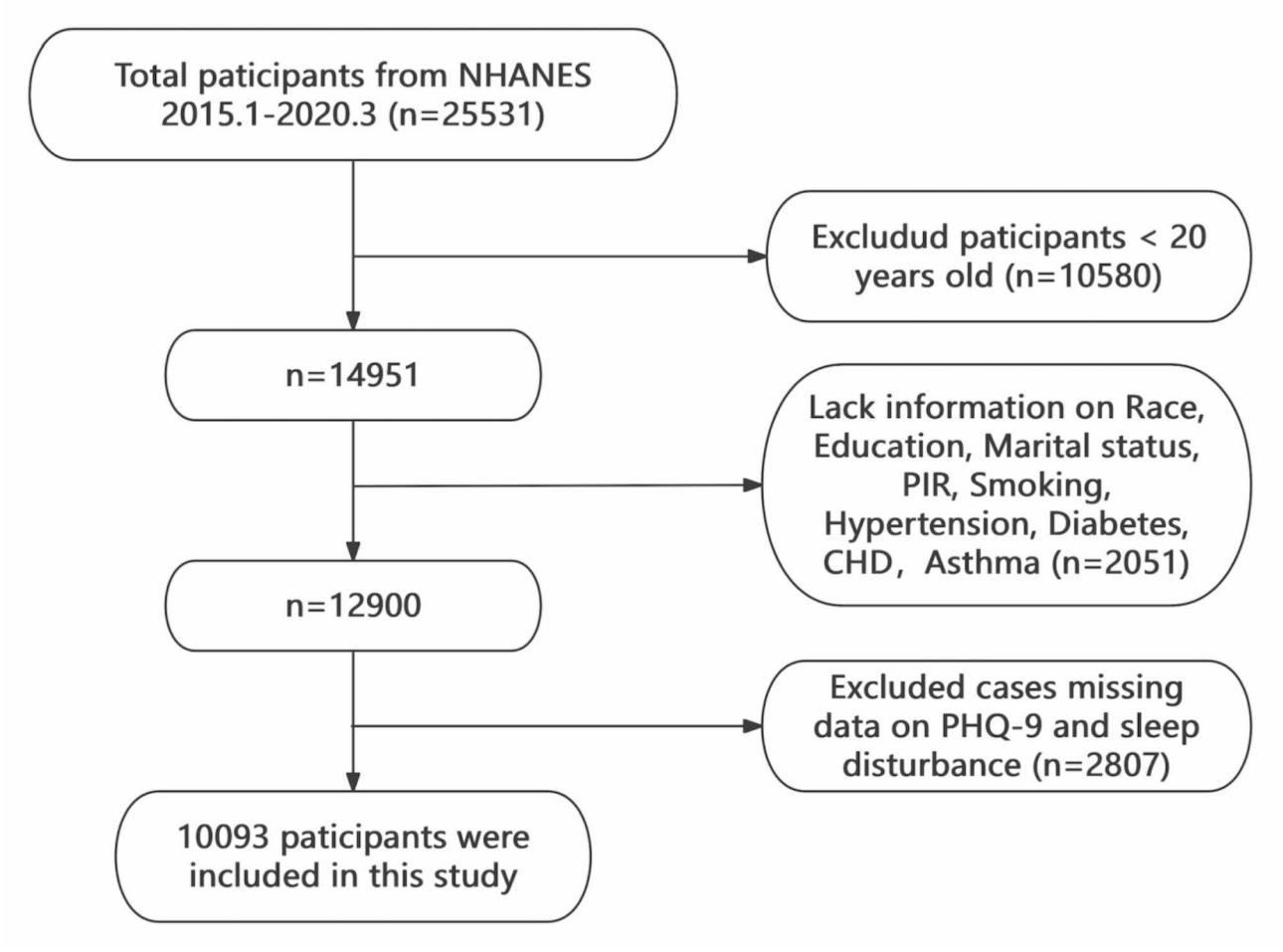

Fig. 1 Flow chart of the screening process from National Health and Nutrition Examination Survey. Abbreviations: PIR, poverty income ratio; CHD, coronary heart disease; PHQ-9, Patient Health Questionnaire-9

Table 1 Definition of sleep quality score

Sleep factors	Sleep condition	Sleep score
Sleep duration (h)	< 7	0
	7–9	1
	> 9	0
Trouble sleeping	No	1
	Yes	0
Snoring	Never	1
	Rarely/occasionally/frequently	0
Excessive daytime sleep	Never/rarely	1
	Rarely/sometimes/occasionally/frequently	0
Sleep apnea symptoms	Never	1
	Rarely/sometimes/occasionally/frequently	0
Sleep quality score	0–5	

daytime sleepiness as metrics. Scores ranged from 0 to 5, with lower scores indicating poorer sleep quality [24]. A sleep quality score below 2 points indicated the presence of sleep disturbances [25].

Assessment of depression

Depression data were derived from the "Mental Health - Depression Screener" dataset within the NHANES questionnaire. Depression severity was assessed using the PHQ-9 questionnaire, a reliable and validated diagnostic tool designed to evaluate mood disorders based

on diagnostic criteria for depression [26]. The questionnaire consists of nine questions, each scored on a scale of 0 to 3, resulting in a total score ranging from 0 to 27. A higher cumulative score signifies increased severity of depression [27, 28].A PHQ-9 total score≥10 is considered indicative of major depressive disorder (MDD) [29].

Potential covariates

Demographic covariates were gathered through household interviews, while health-related covariates were assessed at Mobile Examination Centers (MEC). Age was stratified as <40, 40–60, and >60 years. Race categories were defined as Mexican American, non-Hispanic White, non-Hispanic Black, other Hispanic, and other races. Educational attainment was categorized into three groups: less than high school, high school graduate, and beyond high school. Marital status was classified as never married, married or living with a partner, and widowed, divorced, or separated. Poverty income ratio (PIR) was categorized as <2 (low-income) and ≥2 (moderate to high-income).Participants reporting having smoked at least 100 cigarettes in their lifetime were classified as smokers. Hypertension was determined by clinical diagnosis, ongoing treatment with hypertension medication, or blood pressure readings above 140 mmHg for systolic or 90 mmHg for diastolic pressure measured during the physical assessment. Average blood pressure was calculated from up to three readings taken at different times. The presence of diabetes was confirmed using any of the following criteria: (1) hemoglobin A1C levels at or above 6.5%, or fasting blood glucose levels equal to or exceeding 126 mg/dL [30]; (2) physician-diagnosed diabetes, or use of anti-hyperglycemic medication or insulin. Diagnosis of coronary heart disease (CHD) and asthma was determined based on participants' responses to whether they had ever been diagnosed with these conditions.

Statistical analysis

Given the complex multistage sampling strategy of NHANES, the data were combined and adjusted using the wtmec2 year weighting factor. Baseline characteristics were compared using t-tests for continuous variables and chi-square tests for categorical variables.Continuous data were presented as mean (standard deviation), and categorical data as weighted numbers (weighted percentages). To investigate the association between epilepsy and sleep disturbances, we utilized weighted univariate and multivariate logistic regression analyses. Three models were employed: Model 1, with no covariate adjustments; Model 2, adjusted for age, sex, race, education, marital status, and PIR; and Model 3, which included adjustments for all covariates. Mediation analyses were conducted to explore whether depression mediates the link between epilepsy and sleep disturbance. Subgroup and interaction analyses were employed to investigate associations between epilepsy and various covariates.Findings were presented as odds ratios (ORs) with 95% confidence intervals (CIs). All statistical procedures were conducted using R Studio (version 4.3.2), with a significance level set at $P<0.05$.

Results

Population characteristics

Descriptive statistics of the study are detailed in Table 2. Following a sequence of screening processes, 10,093 individuals were selected from the NHANES database (January 1, 2015 - March 2020), representing a sample of 187,353,423 individuals in the general population. Among these individuals, 73 (weighted count 1,002,936) were diagnosed with epilepsy, while 10,020 (weighted count 186,350,487) were not. Compared to the control group, PWE significantly more frequently experienced MDD (18.84% vs. 7.57%, $P=0.003$) and sleep disturbances (47.17% vs. 15.48%, $P<0.001$). Additionally, there were statistically significant differences in terms of PIR, prevalence of hypertension, diabetes, and asthma, as well as PHQ-9 scores between individuals with and without epilepsy ($P<0.05$).

Weighted logistic regression

We performed weighted univariate and multivariate logistic regression analyses to examine the relationship between epilepsy and sleep disturbance. As shown in Table 3; Fig. 2, the fully adjusted model (Model 3) revealed a robust and statistically significant association between epilepsy and sleep disturbance (OR=3.67, 95% CI=1.68–8.04). Model 3 also indicated a significant relationship between MDD and the occurrence of sleep disturbances (OR=3.32, 95% CI=2.68–4.11).

Mediation analyses

The study evaluated the intermediary role of depression in the relationship between epilepsy and sleep disturbance through a mediation analysis. As depicted in Table 4, mediation effects were observed across all models. Specifically, in Model 1, the mediating impact represented 26.5% of the overall relationship between epilepsy and sleep disturbances (indirect effect=0.053, 95% CI=0.007–0.020, $P<0.001$). In Model 2, with additional adjustments for age, sex, race, education level, marital status, and PIR, the mediation effect constituted 25.4% of the relationship (indirect effect=0.049, 95% CI=0.006–0.020, $P<0.001$). With all covariates adjusted, the mediation effect comprised 23.0% of the total relationship (indirect effect=0.037, 95% CI=0.004–0.015, $P<0.001$).

Table 2 Characteristics of the participants in the NHANES

Variables	Overall		Control Group		Epilepsy Group		*P*-value[d]
	n = 10,093[a]	*n* = 187,353,423[b]	*n* = 10,020[a]	*n* = 186,350,487 [b]	*n* = 73[a]	*n* = 1,002,936 [b]	
Sex							0.6
Female	5,118 (50.71%)	95,652,900 (51.05%)	5,079 (50.69%)	95,087,093 (51.03%)	39 (53.42%)	565,807 (56.42%)	
Male	4,975 (49.29%)	91,700,523 (48.95%)	4,941 (49.31%)	91,263,393 (48.97%)	34 (46.58%)	437,129 (43.58%)	
Age (years)							0.2
<40	3,352 (33.21%)	68,753,487 (36.70%)	3,336 (33.29%)	68,528,511 (36.77%)	16 (21.92%)	224,975 (22.43%)	
40–60	3,648 (36.14%)	70,648,211 (37.71%)	3,621 (36.14%)	70,214,351 (37.68%)	27 (36.99%)	433,860 (43.26%)	
>60	3,093 (30.65%)	47,951,726 (25.59%)	3,063 (30.57%)	47,607,625 (25.55%)	30 (41.10%)	344,101 (34.31%)	
Race							0.4
Mexican American	1,362 (13.49%)	14,955,094 (7.98%)	1,352 (13.49%)	14,883,498 (7.99%)	10 (13.70%)	71,596 (7.14%)	
Other Hispanic	1,111 (11.01%)	12,226,964 (6.53%)	1,101 (10.99%)	12,131,335 (6.51%)	10 (13.70%)	95,629 (9.53%)	
Non-Hispanic white	3,653 (36.19%)	123,612,971 (65.98%)	3,624 (36.17%)	122,988,539 (66.00%)	29 (39.73%)	624,432 (62.26%)	
Non-Hispanic black	2,395 (23.73%)	19,781,239 (10.56%)	2,378 (23.73%)	19,623,729 (10.53%)	17 (23.29%)	157,510 (15.70%)	
Other race	1,572 (15.58%)	16,777,155 (8.95%)	1,565 (15.62%)	16,723,386 (8.97%)	7 (9.59%)	53,769 (5.36%)	
Education							0.3
Less than high school	1,843 (18.26%)	19,838,777 (10.59%)	1,829 (18.25%)	19,718,999 (10.58%)	14 (19.18%)	119,778 (11.94%)	
High school	2,307 (22.86%)	45,250,047 (24.15%)	2,285 (22.80%)	44,907,803 (24.10%)	22 (30.14%)	342,244 (34.12%)	
High school or above	5,943 (58.88%)	122,264,599 (65.26%)	5,906 (58.94%)	121,723,685 (65.32%)	37 (50.68%)	540,914 (53.93%)	
Marital status							0.2
Never married	1,869 (18.52%)	33,231,505 (17.74%)	1,849 (18.45%)	32,948,958 (17.68%)	20 (27.40%)	282,547 (28.17%)	
Widowed、Divorced、Separated	1,987 (19.69%)	30,231,818 (16.14%)	1,970 (19.66%)	30,034,550 (16.12%)	17 (23.29%)	197,268 (19.67%)	
Married、Living with partner	6,237 (61.80%)	123,890,100 (66.13%)	6,201 (61.89%)	123,366,979 (66.20%)	36 (49.32%)	523,121 (52.16%)	
PIR							< 0.001
<2	4,610 (45.68%)	58,506,857 (31.23%)	4,563 (45.54%)	57,871,642 (31.06%)	47 (64.38%)	635,216 (63.34%)	
≥ 2	5,483 (54.32%)	128,846,566 (68.77%)	5,457 (54.46%)	128,478,845 (68.94%)	26 (35.62%)	367,721 (36.66%)	
Smoking							0.6
No	5,844 (57.90%)	107,435,355 (57.34%)	5,809 (57.97%)	106,895,472 (57.36%)	35 (47.95%)	539,882 (53.83%)	
Yes	4,249 (42.10%)	79,918,069 (42.66%)	4,211 (42.03%)	79,455,015 (42.64%)	38 (52.05%)	463,054 (46.17%)	
Hypertention							0.009
No	5,783 (57.30%)	117,566,199 (62.75%)	5,754 (57.43%)	117,168,625 (62.88%)	29 (39.73%)	397,574 (39.64%)	
Yes	4,310 (42.70%)	69,787,224 (37.25%)	4,266 (42.57%)	69,181,862 (37.12%)	44 (60.27%)	605,362 (60.36%)	
Diabetes							< 0.001
No	8,160 (80.85%)	159,968,221 (85.38%)	8,111 (80.95%)	159,352,069 (85.51%)	49 (67.12%)	616,152 (61.43%)	

Table 2 (continued)

Variables	Overall		Control Group		Epilepsy Group		*P*-value[d]
	n = 10,093[a]	*n* = 187,353,423[b]	*n* = 10,020[a]	*n* = 186,350,487 [b]	*n* = 73[a]	*n* = 1,002,936 [b]	
Yes	1,933 (19.15%)	27,385,202 (14.62%)	1,909 (19.05%)	26,998,418 (14.49%)	24 (32.88%)	386,784 (38.57%)	
CHD							0.4
No	9,662 (95.73%)	180,160,819 (96.16%)	9,595 (95.76%)	179,225,292 (96.18%)	67 (91.78%)	935,527 (93.28%)	
Yes	431 (4.27%)	7,192,604 (3.84%)	425 (4.24%)	7,125,194 (3.82%)	6 (8.22%)	67,409 (6.72%)	
Asthma							0.006
No	8,532 (84.53%)	158,714,524 (84.71%)	8,480 (84.63%)	158,020,820 (84.80%)	52 (71.23%)	693,704 (69.17%)	
Yes	1,561(15.47%)	28,638,899 (15.29%)	1,540 (15.37%)	28,329,667 (15.20%)	21 (28.77%)	309,233 (30.83%)	
PHQ-9 score[c]	3.07 (4.00)		3.05 (3.98)		5.49 (5.33)		0.039
MDD							0.003
No	9,266 (91.81%)	173,052,287 (92.37%)	9,209 (91.91%)	172,238,327 (92.43%)	57 (78.08%)	813,961 (81.16%)	
Yes	827 (8.19%)	14,301,136 (7.63%)	811 (8.09%)	14,112,160 (7.57%)	16 (21.92%)	188,976 (18.84%)	
Sleep disturbance							< 0.001
No	8,505 (84.27%)	158,025,084 (84.35%)	8,458 (84.41%)	157,495,217 (84.52%)	47 (64.38%)	529,867 (52.83%)	
Yes	1,588 (15.73%)	29,328,340 (15.65%)	1,562 (15.59%)	28,855,270 (15.48%)	26 (35.62%)	473,070 (47.17%)	

Abbreviations: PIR, poverty income ratio; CHD, coronary heart disease; PHQ-9, Patient Health Questionnaire-9; MDD, major depressive disorder

[a]n (percentages); [b]weighted n (weighted percentages); [c]Mean (SD)

[d] chi-squared test with Rao & Scott's second-order correction; Wilcoxon rank-sum test for complex survey sample

Table 3 Associations of sleep disturbance with epilepsy and depression

	Model 1		Model 2		Model 3	
	OR(95% CI)	*P*	OR(95% CI)	*P*	OR(95% CI)	*P*
Epilepsy						
No	Ref.		Ref.		Ref.	
Yes	4.87 (2.50, 9.50)	<0.001	4.43 (2.19, 8.93)	<0.001	3.67 (1.68, 8.04)	0.002
PHQ-9	1.15 (1.13, 1.17)	<0.001	1.16 (1.14, 1.18)	<0.001	1.14 (1.12, 1.16)	<0.001
MDD						
No	Ref.		Ref.		Ref.	
Yes	3.93 (3.14, 4.92)	<0.001	4.04 (3.21, 5.08)	<0.001	3.32 (2.68, 4.11)	<0.001

Model 1: No covariate were adjusted. Model 2: Adjusted for age, sex, race, education, marital status and PIR. Model 3: Adjusted for age, sex, race, education, marital status, PIR, smoking status, diabetes, hypertension, CHD, asthma.Abbreviations: PHQ-9, Patient Health Questionnaire-9; MDD, major depressive disorder

Stratified analyses and interaction analyses

Subgroup analysis elucidated the heterogeneity in the association between epilepsy and sleep disturbances across various demographic strata (Fig. 3). Notably, substantial disparities were identified among subgroups delineated by sex, age, race, educational level, marital status, PIR, smoking status, and the presence of hypertension, diabetes, CHD, and asthma (all $P<0.05$). Specifically, significant differences were detected among males, females, those younger than 40 years, individuals aged 40–60 years, Mexican Americans, non-Hispanic whites, non-Hispanic blacks, individuals with education beyond high school and those with education lower than high school, those who were married or living with a partner, those with a PIR lower than 2, smokers, and those not suffering from hypertension, diabetes, CHD, or asthma. In the analysis of the interaction effects on subgroups, age ($P=0.049$) and hypertension ($P=0.045$) were found to interact with epilepsy. Participants under 40 years of age (OR = 3.50, 95% CI = 1.17–10.47, $P=0.025$) and those aged 40–60 years (OR = 4.22, 95% CI = 1.90–9.34, $P<0.001$) had a higher risk of sleep disturbance compared to those over 60 years old. Participants without hypertension (OR = 4.45, 95% CI = 2.05–9.68, $P<0.001$) showed a higher risk of sleep disturbance compared to those with hypertension.

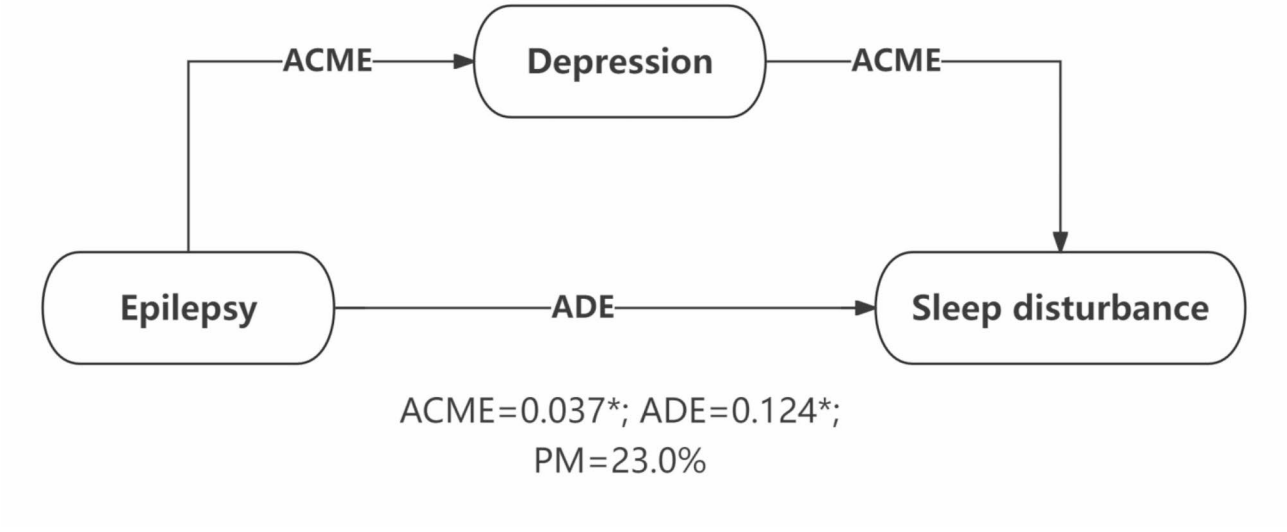

Fig. 2 Mediational models. Abbreviations: ACME, average causal mediation effects; ADE, average direct effects; PM, proportion mediated.*indicates $P<0.01$

Discussion

Our research investigated the connection between epilepsy and sleep disturbances using NHANES data. After adjusting for all confounders, we revealed a higher prevalence of sleep disturbance in PWE, which was consistent with prior research [31, 32]. Furthermore, mediation models highlighted that depression was significantly correlated with sleep disturbances in the adult American population.

A multitude of studies have documented a significant link between depressive states and disruptions in sleep [33]. Lin et al. identified several shared genetic variations, including MEIS1, OLFM4, and HEXIM1, that link MDD with insomnia [34]. Zhao et al. conducted research on 3,275 MDD patients at 32 different sub-centers, uncovering that more than 70% suffered from sleep disturbances [35]. Our data reaffirmed this association. In a retrospective and prospective collaborative study, it was found that higher depression scores could predict sleep disturbances in PWE [36]. Some researchers believe that depression, rather than epilepsy itself, is the main cause of sleep disturbances [37], which contradicts our findings. We identified epilepsy as an important contributing factor to sleep disturbances, with depression mediating approximately 23.0–26.5% of the relationship between epilepsy and sleep disturbances across various mediation models.

Epilepsy patients are at an elevated risk of experiencing sleep disturbances. Due to the considerable risks posed by comorbid conditions, extensive research has been conducted into the causes of the concurrent presence of epilepsy and sleep disorders, as well as the exploration of preventive measures [38]. Our study revealed that the prevalence of sleep disturbances among epilepsy patients was strikingly high at 47.17%, significantly exceeding that observed in the control group. A cross-sectional study indicated that 50.4% of epilepsy patients reported suffering from insomnia [39]. In a meta-analysis encompassing 25 original studies, Bergmann et al. revealed that epilepsy patients had notably higher Pittsburgh Sleep Quality Index scores than their counterparts [40]. Epileptic seizures often manifest during sleep, and recurrent episodes can disrupt sleep microstructure, hindering the progression from light to deep sleep stages, thus impacting both the quality and duration of sleep [41]. Certain antiepileptic drugs such as barbiturates and phenytoin may directly alter sleep patterns, induce drowsiness, reduce sleep quality, or trigger other related issues [42, 43].

Through subgroup analysis and interaction tests, we identified significant interactions between age, hypertension, and epilepsy regarding sleep disturbances. Our study findings indicate that epilepsy significantly increases the risk of sleep disturbance in individuals aged ≤ 60 years, whereas the association is not evident in individuals aged > 60 years. Possible explanations include age-related alterations in sleep architecture, coupled with the influence of physiological changes and comorbid chronic conditions [44, 45].It is important to recognize that although our findings reveal that the likelihood of sleep disturbances in epilepsy patients without hypertension is 4.45 times higher than in patients without epilepsy, this association is weakened among patients with hypertension. One must be cautious in interpreting these observations. Certain antihypertensive medications, including Alpha-2 agonists, can regulate the sleep structure of patients [46]. Additionally, hypertension often coexists with cardiovascular and cerebrovascular

Table 4 Depression mediating the association between epilepsy and sleep disturbance

	ACME				ADE				Total effect				Proportion mediated			
	Estimate	95%CI lower	95%CI upper	*P*-value	Estimate	95%CI lower	95%CI upper	*P*-value	Estimate	95%CI lower	95%CI upper	*P*-value	Estimate	95%CI lower	95%CI upper	*P*-value
Model 1	0.053	0.007	0.020	<0.001	0.147	0.066	0.228	<0.001	0.200	0.117	0.284	<0.001	0.265	0.117	0.648	<0.001
Model 2	0.049	0.006	0.020	<0.001	0.144	0.063	0.224	<0.001	0.193	0.109	0.277	<0.001	0.254	0.112	0.395	<0.001
Model 3	0.037	0.004	0.015	<0.001	0.124	0.044	0.204	0.002	0.161	0.078	0.243	<0.001	0.230	0.071	0.379	<0.001

Model 1: No covariate were adjusted. Model 2: Adjusted for age, sex, race, education, marital status and PIR. Model 3: Adjusted for age, sex, race, education, marital status, PIR, smoking status, diabetes, hypertension, CHD, asthma. Abbreviations: ACME, average causal mediation effect; ADE, average direct effect

diseases [47, 48], obesity [49], and multiple comorbidities [50], potentially contributing to an elevated prevalence of sleep disturbances among hypertensive individuals, irrespective of epilepsy diagnosis. Moreover, elevated blood pressure can result in compromised regulation of cerebral blood flow [51] and perturb the equilibrium of neurotransmitters in the brain, thereby disrupting typical sleep patterns. Hence, the link between epilepsy, hypertension, and sleep disturbances may be attributed to a shared pathophysiological mechanism rather than a direct causal link.

Our study utilized a large dataset representing a national population sample to confirm that depression is a significant factor contributing to sleep disturbances in PWE. Additionally, we investigated the effects of multiple factors such as age, racial background, and the presence of hypertension. Disturbances in sleep can profoundly affect the well-being of individuals with epilepsy and have been associated with a wide range of health concerns, as indicated by prior research [52, 53]. Addressing depressive symptoms may lead to improvements in sleep quality and, consequently, promote the overall health and well-being of individuals in this patient population.

Despite the findings, our research is subject to constraints. Primarily, the cross-sectional design prevents the determination of cause-and-effect relationships between epilepsy, depressive symptoms, and sleep disturbances. Furthermore, our selection criteria, based on pre-existing data, may not fully represent the entire epilepsy patient population. Some individuals may not have undergone standardized antiepileptic medication therapy, and some patients with a history of epilepsy did not take antiepileptic medications within the last 30 days of the survey. Additionally, the study did not consider the impact of antiepileptic drugs on sleep and depression, nor did it include key variables such as epilepsy duration, types of seizures, and seizure frequency, which were absent due to insufficient NHANES data. Another limitation arises from our reliance on self-reported assessments of sleep disturbances, lacking objective measures such as actigraphy or polysomnography, potentially introducing reporting bias. Furthermore, the use of the PHQ-9 for diagnosing depression lacks clinical confirmation. These limitations should be considered and addressed in future research.

Conclusion

This investigation reveals a strong correlation between epilepsy and the occurrence of sleep disturbances. The role of depression as a key factor in this correlation underscores the intricate links between epilepsy, psychological health, and sleep disturbances. Despite these insights, additional research is necessary to determine causal relationships and to explore the potential

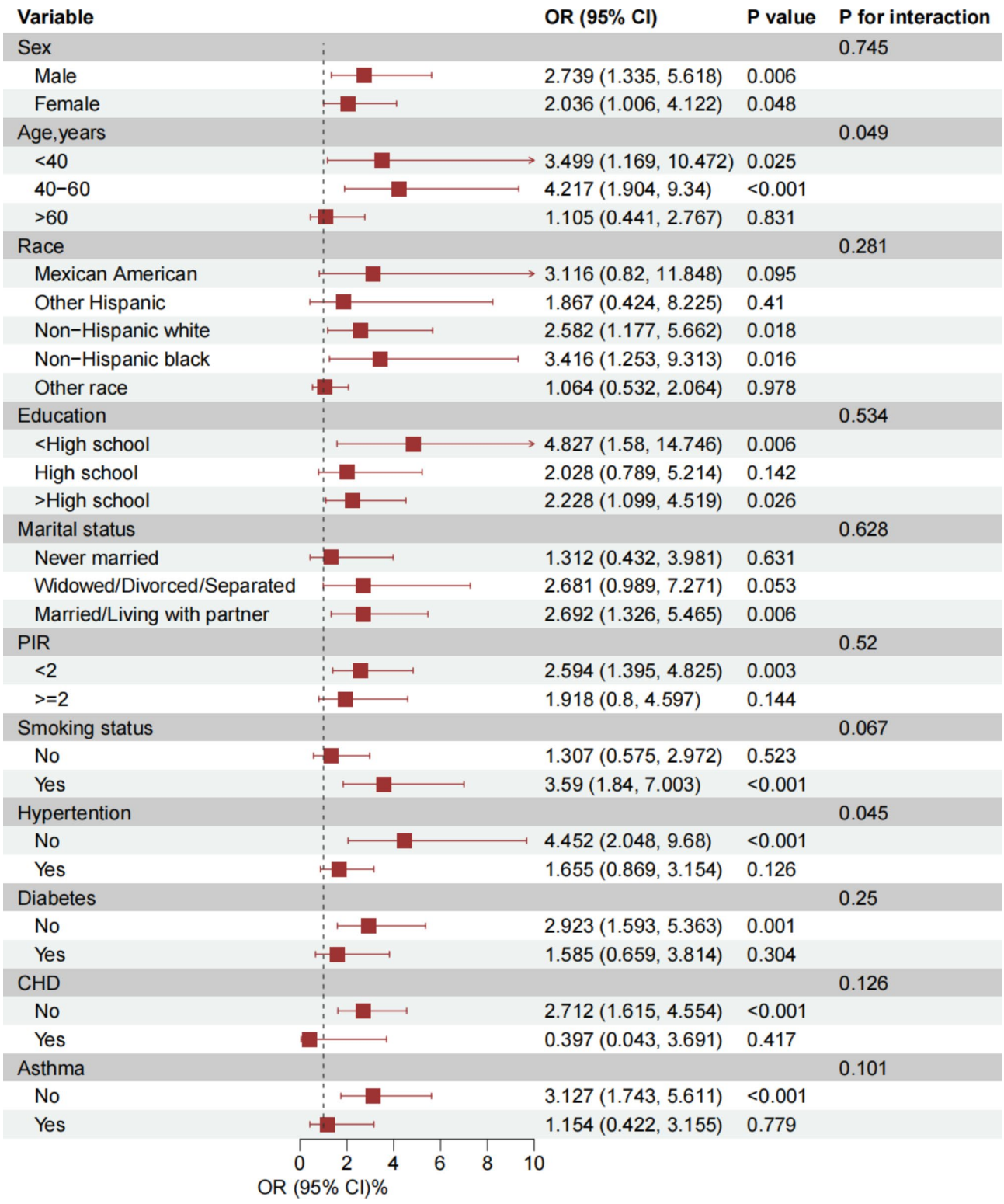

Fig. 3 Subgroup analysis of the association between epilepsy and sleep disturbance. Eachstratification was adjusted for sex, age, race, education level, marital status, PIR, smoking status, hypertension, diabetes, CHD and asthmaexcept the stratification factor itself. Abbreviations: PIR, poverty income ratio; CHD, coronary heart disease

mechanisms. Furthermore, expanded prospective studies are required to confirm these observations and to guide the development of more precise strategies for enhancing sleep and overall health in the epileptic population.

Abbreviations

PWE	People with epilepsy
MDD	Major depressive disorder
PHQ-9	Patient Health Questionnaire-9
PIR	Poverty income ratio
CHD	Coronary heart disease
NHANES	National health and nutrition examination survey
MEC	Mobile examination center
OR	Odds ratio
CI	Confidence interval
ACME	Average causal mediation effects
ADE	Average direct effects
PM	Proportion mediated

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-19898-5.

Supplementary Material 1

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Author contributions

Qianhui Wen conceptualized the research, conducted the preliminary analysis, and drafted the initial manuscript. Qian Wang reviewed and revised the manuscript. Hua Yang was responsible for the study supervision and data collection. All authors read and approved the final manuscript.

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Data availability

Additional details about the NHANES database are available on the official website at www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

Ethical clearance for this study was obtained from the National Center for Health Statistics Ethics Review Committee, and all methods were conducted in line with the principles outlined in the Declaration of Helsinki. Prior to their involvement, participants gave their voluntary and informed consent in written form.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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