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# Factors contributing to excessive daytime sleepiness in Korean adults with epilepsy: A sleep questionnaire-based study

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ABSTRACT

*Objectives:* We determined factors contributing to excessive daytime sleepiness (EDS) in Korean adults with epilepsy (AWE).

*Methods:* A total of 147 AWE who had been treated for >1 year were included. Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS). Subjective sleep disturbances were assessed with the Sleep Apnea of Sleep Disorder Questionnaire (SA-SDQ) and questionnaires about insomnia and restless legs syndrome (RLS). The Hospital Anxiety and Depression Scale (HADS) was also used. An ESS score >10 was considered indicative of EDS. Multivariate logistic regression analyses using the backward elimination method were performed for variables with a $p < 0.10$ on univariate analysis.

*Results:* The mean ESS score was 6.8 (standard deviation [SD]: 4.4). Among the 147 subjects, 36 (24.5%) had EDS. Multivariate logistic regression analysis showed that being employed (odds ratio [OR]: 4.469, $p < 0.01$), the presence of at least one sleep disturbance (OR: 3.626, $p < 0.01$), and antiepileptic drug (AED) polytherapy (OR: 2.663, $p < 0.05$) were independently associated with EDS in the overall group of AWE. In contrast, being employed ($p < 0.05$) and higher Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) scores ($p < 0.05$) in a model for men with epilepsy, as well as having at least one sleep disturbance ($p < 0.05$) in a model for women with epilepsy, were identified as independent factors for EDS.

*Conclusions:* Excessive daytime sleepiness in AWE may have a multifactorial origin. Being employed, subjective sleep disturbances, and AED polytherapy are independent predictors of EDS. There may be sex differences in factors associated with EDS.

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## 1. Introduction

Epilepsy is frequently accompanied by sleep disturbance. A prospective study showed that poor sleep quality, difficulty sleeping, and obstructive sleep apnea (OSA) were two to three times more common in adults with epilepsy (AWE) than in healthy controls [1]. Such sleep disturbance may have a significant negative effect on mood and quality of life [2,3]. In addition, a reciprocal interaction between sleep and epilepsy was recognized long ago, as sleep disturbance can provoke seizures, and epilepsy itself can disrupt sleep [4].

Excessive daytime sleepiness (EDS) is one of the most frequent sleep-related complaints in AWE. It can be measured by the Epworth Sleepiness Scale (ESS), which is the most common instrument used in sleep research [5,6]. While sleep disturbance in AWE had been consistently demonstrated [1–3], the prevalence of EDS in AWE reportedly varies from 10% to 48% [7]. In some studies, the prevalence of an ESS score >10 in AWE was similar to that in controls [1,2,8,9], but others have reported a higher prevalence in AWE [3,10–12]. The etiology of EDS in epilepsy has not been clarified, but it may be multifactorial, including epilepsy-related factors, psychological distress, and coexisting sleep disorders [7]. Frequent seizures during sleep may directly disrupt sleep, and the effects of antiepileptic drugs (AEDs) may do so indirectly [8,9]. Psychological problems such as depression and anxiety are frequently present in AWE and may contribute significantly to sleep disturbance [13,14]. A recent systematic literature review found that EDS in epilepsy seems to be more related to undiagnosed sleep disorders than to epilepsy-related factors [7]. Treatment of the sleep disorders may therefore be expected to improve EDS.

It is possible that factors contributing to EDS in epilepsy differ depending on the reported prevalence in various studies. For example,

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when the prevalence of an ESS score >10 in AWE was reportedly comparable with that of controls, symptoms suggestive of OSA and restless legs syndrome (RLS) were stronger predictors of EDS than frequency of seizures or the AEDs used [8,9]. In contrast, a study showing a higher prevalence of an ESS score >10 (45%) also had a trend for higher scores of daytime sleepiness in patients with intractable seizures [12]. We previously reported EDS in 25.2% of Korean AWE, the prevalence no different than in healthy controls [15]. Therefore, we designed a questionnaire-based study to evaluate factors that might contribute to EDS in Korean AWE. We included employment status as one of the variables because it might particularly contribute to EDS in a country where long working hours are recognized as a social problem.

## 2. Materials and methods

### 2.1. Subjects

This cross-sectional, multicenter study was conducted using a database constructed for a previous study of the prevalence of subjective sleep disturbances and their impact on health-related quality of life in persons with epilepsy [15]. Participants were recruited from the neurologic outpatient clinics of five university hospitals in Korea. Individuals >18 years of age who had been diagnosed with epilepsy and had been treated for >1 year at the time of recruitment were eligible to participate. Adults with epilepsy were excluded if they had a neurological deficit (such as hemiparesis, ataxia, gait problems, or cognitive impairment), medical disorder, or psychiatric disorder that negatively impact psychological distress beyond the effects of epilepsy. Such decision was made by the epileptologists who have treated an individual patient. We did not exclude patients whose Hospital Anxiety and Depression Scale (HADS) scores were over the thresholds for psychological distress if they had not been diagnosed with a psychiatric disorder or if they were taking regular medication for the treatment of their condition. We also excluded AWE who had a seizure except simple partial seizures or myoclonic seizures in the 48 h prior to filling out the questionnaires, in order to avoid influences of postictal behavior symptoms, with the following rationale. In a prior study [16], postictal behavior symptoms were evaluated in a systematic manner, and the median duration of two-thirds of postictal symptoms was found to be 24 h. Therefore, the postictal period in this study was defined as the 48 h after a seizure. To avoid potential influences of circadian rhythm disorders, AWE who were shift workers or who worked later than 8 p.m. were also excluded. Finally, AWE were excluded if they had difficulty with conversation or written communication.

Participants who fulfilled the inclusion criteria and agreed to join the study were asked to fill out questionnaires on the day they visited an outpatient clinic. All participants indicated whether they were regularly taking hypnotics or sedative drugs to treat a sleep disturbance. Demographic and clinical data were collected by interview and from information in medical files. Written informed consent was obtained from all study participants. The study was reviewed and approved by the Institutional Review Board of the Asan Medical Center.

### 2.2. Measures

Daytime sleepiness was assessed using the ESS [15], consisting of eight questions about how often a person dozed during daily activities. The answers were on a 4-point scale ranging from 0 (never dozed) to 3 (high chance of dozing), with total possible scores ranging from 0 to 24. Higher scores indicate greater sleep propensity during the day. An ESS score >10 is considered indicative of EDS. The validated Korean version of the ESS was used in this study [17].

Respondents were asked to answer yes or no to questions about insomnia symptoms. Insomnia symptoms were defined as present if a patient had any one of three complaints lasting longer than one month and occurring at least once a week. These included 1) difficulty falling asleep, 2) difficulty maintaining sleep (i.e., waking up during the night with difficulty getting back to sleep), and 3) waking up too early in the morning and being unable to return to sleep.

Obstructive sleep apnea was assessed using the Sleep Apnea of Sleep Disorder Questionnaire (SA-SDQ) [18]. It consists of eight questions and four items related to weight, smoking status, age, and body mass index, with the responses calculated to generate a raw score. The eight questions address specific symptoms of sleep apnea syndrome including loud snoring, arrested breathing while asleep at night, awaking suddenly gasping for breath, sweating during sleep, high blood pressure, blocked nose when trying to sleep, snoring, breathing worse when lying supine, and snoring or breathing during sleep worsening after alcohol use. Total scores range from 0 to 60. The SA-SDQ is a standard screening questionnaire for OSA in Korea [19]. To identify patients with suspected OSA, we used cutoff points of 29 for men and 26 for women, as has been suggested for people with epilepsy [20].

The questionnaire on RLS symptoms inquired about three key symptoms: 1) an urge to move the legs, usually accompanied by or thought to be caused by uncomfortable and unpleasant sensations in the legs; 2) the sensations beginning or worsening during periods of rest or inactivity, such as lying down or sitting, with at least temporary relief by movement, such as walking or stretching, and 3) occurring exclusively or predominantly in the evening or night rather than during the day. Only patients who had all three symptoms were considered to have RLS.

Subjective sleep quantity was measured by a single question: "on the average, how many hours did you sleep each night during the past 4 weeks?"

Symptoms of anxiety and depression were measured using the Korean version of the HADS [21]. This tool consists of 14 items, seven related to anxiety (HADS-A subscale) and seven related to depression (HADS-D subscale). Items are scored on a scale of 0 (no distress) to 3 (significant distress), generating a maximum score of 21 for each subscale. Higher scores indicate higher levels of depression or anxiety.

### 2.3. Statistical analysis

Data are presented as mean and standard deviation (SD) for numeric variables and numbers and percentages for nominal variables. All statistical tests were two-tailed, and $p < 0.05$ was considered significant. The dependent variable was the presence or absence of EDS, defined as an ESS score >10. The independent variables included sociodemographic, epilepsy-related, sleep-related, and neuropsychological factors. Sociodemographic variables were age, sex, body mass index, and employment status. Both students and housewives were considered to be employed, because they typically work or study in a manner similar to that of self-employed individuals in Korea. Epilepsy-related variables were age at seizure onset, duration of epilepsy, type of epilepsy and seizures, seizure frequency, being seizure-free for at least one year, recurrence of generalized tonic–clonic seizures in the prior two years, nocturnal seizures with more than 90% of seizures occurring during sleep, and AED treatment (AED monotherapy vs. polytherapy). The number of seizures occurring in the prior year was counted via medical chart; seizure frequency was assessed as a categorical variable because the number of seizures was not distributed normally. Sleep-related variables were subjective sleep quantity and the presence or absence of the OSA, insomnia symptoms, and RLS symptoms. Neuropsychological variables comprised the HADS-A and HADS-D scores. Univariate analyses were conducted using an unpaired *t*-test for continuous variables and a chi-squared test or Fisher's exact test for categorical variables. Variables with $p < 0.10$ on univariate analysis were then entered into multivariate logistic regression models to assess variables associated with EDS. The backward elimination method for variable selection was used with exit criteria of $p > 0.10$ and entry criteria of $p < 0.05$. A concordance statistic (c-statistic) was calculated. The c-statistics assessed the discrimination of the model (i.e.,

**Table 1**
Subject characteristics (n = 147).

| | |
|---|---|
| Male, n (%) | 73 (49.7) |
| Age, years, mean (SD) | 37.2 (10.4) |
| Body mass index, kg/m$^2$, mean (SD) | 27.0 (7.0) |
| Unemployed, n (%) | 45 (30.6) |
| Seizure onset, years, mean (SD) | 22.1 (13.1) |
| Epilepsy duration, years, mean (SD) | 15.4 (9.0) |
| Epilepsy syndrome, n (%) | |
| Idiopathic generalized | 27 (18.4) |
| Symptomatic/cryptogenic partial | 103 (70.1) |
| Undetermined | 17 (11.6) |
| Predominant seizure type, n (%) | |
| Simple partial | 16 (11.4) |
| Complex partial | 63 (45.0) |
| Generalized tonic–clonic | 61 (43.6) |
| Seizure frequency in the last year, n (%) | |
| Seizure-free | 63 (42.9) |
| <1/month | 59 (40.1) |
| ≥1/month | 25 (17.0) |
| GTCS in the last year, n (%) | 90 (61.2) |
| Nocturnal seizures >90%, n (%) | 27 (18.4) |
| Monotherapy, n (%) | 73 (49.7) |
| HADS-A subscale, mean (SD) | 6.8 (3.6) |
| HADS-A scores >7, n (%) | 58 (39.5) |
| HADS-D subscale, mean (SD) | 6.6 (4.0) |
| HADS-D scores >7, n (%) | 61 (41.5) |
| Subjective sleep disturbance, n (%) | 64 (43.5) |
| Insomnia symptoms, n (%) | 52 (35.4) |
| Sleep disordered breathing, n (%) | 34 (23.1) |
| Male/female, n (%) | 21 (28.8%)/13 (17.6%) |
| RLS symptoms, n (%) | 11 (7.5) |
| Subjective sleep quantity, h, mean (SD) | 6.9 (1.6) |

GTCS, generalized tonic–clonic seizures; HADS-D, Hospital Anxiety and Depression Scale-Depression subscale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety subscale; RLS, restless legs syndrome; SD, standard deviation.
Continuous variables are shown as mean (SD) and categorical variables are shown as n (%).

the ability of the model to distinguish patients who had EDS from those who did not). In the current study, the calibration power of each model was assessed by using the Hosmer–Lemeshow goodness of fit test. $p > 0.05$ indicated a well-calibrated model.

## 3. Results

### 3.1. Subject characteristics

A total of 147 participants were included in this study (Table 1), of whom 36 (24.5%) had EDS, defined as an ESS score >10. The mean age was 37.2 years old (SD: 10.4). Nearly half (n = 73, 49.7%) took one AED, 49 (43.3%) took two, 15 (10.2%) took three, and 10 (6.8%) took four or more. Antiepileptic drugs prescribed for more than 10% of participants included valproic acid (37.4%), lamotrigine (30.6%), carbamazepine (28.6%), oxcarbazepine (25.2%), topiramate (15.0%), levetiracetam (14.3%), and phenytoin (10.9%). Only eight (5.4%) reported regularly taking hypnotics or sedative drugs to treat a sleep disturbance, in which benzodiazepine for seizure control was not included.

### 3.2. Factors associated with EDS in AWE

Excessive daytime sleepiness was significantly associated with being employed ($p < 0.05$), having at least one sleep disturbance ($p < 0.05$), and higher HADS-A scores ($p < 0.05$) (Table 2) in the overall group of AWE. Men with epilepsy showed significant associations of EDS solely with being employed ($p < 0.05$) and higher HADS-A scores ($p < 0.05$) whereas women with epilepsy showed a significant association of EDS solely with having at least one sleep disturbance ($p < 0.05$). Subjective sleep quantity tended to be shorter in men (mean: 6.7 h, SD: 1.5) than in women (mean: 7.2 h, SD: 1.7) ($p = 0.082$). However, subjective sleep quantity did not differ between participants with and without EDS, or between employed and unemployed participants. Adults with epilepsy with insomnia symptoms had higher scores of HADS-A ($9.8 \pm 4.6$ vs. $5.2 \pm 3.5$, $p < 0.001$) and HADS-D ($9.0 \pm 3.8$ vs. $5.7 \pm 3.3$, $p < 0.001$) than those without insomnia symptoms. There were no significant differences between those with and without EDS in terms of other variables that were assessed.

Multivariate logistic regression analysis showed that being employed (odds ratio [OR]: 4.469, $p < 0.01$), the presence of at least one sleep disturbance (OR: 3.626, $p < 0.01$), and AED polytherapy (OR: 2.663, $p < 0.05$) were independently associated with EDS in the overall group of AWE (Table 3). The Hosmer–Lemeshow test revealed that the model fit well ($p = 0.402$); the model for EDS had good discrimination (a c-statistic of 0.717). In contrast, independent factors for EDS were identified as being employed ($p < 0.05$) and higher HADS-A scores ($p < 0.05$) in a model for men with epilepsy ($p = 0.762$ for the Hosmer–Lemeshow test and a c-statistic of 0.780) whereas independent factors for EDS were identified as having at least one sleep disturbance ($p < 0.05$) in a model for women with epilepsy ($p = 0.993$ for the Hosmer–Lemeshow test and a c-statistic of 0.654). In men with epilepsy, AED polytherapy ($p = 0.073$) lost statistical significance for EDS. When specific types of sleep disturbances were entered individually into the multivariate analysis, none were significantly related to EDS.

**Table 2**
Univariate comparisons of variables between subjects with and without excessive daytime sleepiness.

| | Total (n = 147) | | | Men (n = 73) | | | Women (n = 74) | | |
|---|---|---|---|---|---|---|---|---|---|
| | EDS (n = 36) | No EDS (n = 111) | p value | EDS (n = 19) | No EDS (n = 54) | p value | EDS (n = 17) | No EDS (n = 57) | p value |
| Employed, n (%) | 30 (83.3) | 72 (64.9) | 0.037 | 17 (89.5) | 34 (63.0) | 0.030 | 13 (76.5) | 38 (66.7) | 0.443 |
| Having ≥1 sleep disturbance[a], n (%) | 23 (63.9) | 41 (36.9) | 0.005 | 13 (68.4) | 25 (46.3) | 0.097 | 10 (58.8) | 16 (28.1) | 0.020 |
| Sleep disordered breathing, n (%) | 11 (30.6) | 23 (20.7) | 0.224 | 6 (31.6) | 15 (27.8) | 0.753 | 5 (29.4) | 8 (14.0) | 0.160 |
| Insomnia symptoms, n (%) | 17 (47.2) | 35 (31.5) | 0.087 | 10 (52.6) | 21 (38.9) | 0.297 | 7 (41.2) | 14 (24.6) | 0.224 |
| RLS symptoms, n (%) | 5 (13.9) | 6 (5.4) | 0.093 | 1 (5.3) | 2 (3.7) | 1.000 | 4 (23.5) | 4 (7.0) | 0.076 |
| Subjective sleep quantity, h, mean (SD) | 6.86 (1.82) | 6.96 (1.53) | 0.774 | 6.63 (1.77) | 6.72 (1.41) | 0.208 | 7.15 (1.91) | 7.22 (1.62) | 0.901 |
| AED polytherapy, n (%) | 23 (63.9) | 51 (45.9) | 0.061 | 11 (57.9) | 22 (40.7) | 0.196 | 12 (70.6) | 29 (50.9) | 0.151 |
| Age at seizure onset, year, mean (SD) | 19.7 (10.3) | 22.6 (13.6) | 0.180 | 20.4 (12.1) | 23.9 (14.7) | 0.356 | 18.9 (8.0) | 21.3 (12.5) | 0.344 |
| Duration of epilepsy, year, mean (SD) | 16.5 (7.5) | 15.3 (9.8) | 0.451 | 16.5 (7.8) | 14.9 (9.8) | 0.518 | 16.5 (7.4) | 15.8 (9.9) | 0.765 |
| 1-Year seizure remission, n (%) | 15 (41.7) | 48 (43.2) | 0.868 | 10 (52.6) | 23 (42.6) | 0.450 | 5 (29.4) | 25 (43.9) | 0.287 |
| GTCS in the prior 2 years, n (%) | 20 (55.6) | 70 (63.1) | 0.422 | 9 (47.4) | 37 (68.5) | 0.101 | 11 (64.7) | 33 (57.9) | 0.616 |
| >90% nocturnal seizures, n (%) | 5 (13.9) | 22 (19.8) | 0.425 | 5 (26.3) | 13 (24.1) | 0.845 | 0 (0.0) | 9 (15.8) | 0.107 |
| IGE, n (%) | 9 (25.0) | 18 (16.2) | 0.237 | 6 (31.6) | 11 (20.4) | 0.320 | 3 (17.6) | 7 (12.3) | 0.687 |
| HADS-D subscale, mean (SD) | 7.6 (3.5) | 6.5 (3.7) | 0.130 | 7.9 (3.5) | 6.6 (3.6) | 0.186 | 7.2 (3.7) | 6.4 (3.7) | 0.453 |
| HADS-A subscale, mean (SD) | 7.9 (4.2) | 6.2 (3.9) | 0.043 | 8.5 (4.4) | 6.3 (3.8) | 0.047 | 7.3 (4.1) | 6.2 (4.4) | 0.403 |

AED, antiepileptic drug; EDS, excessive daytime sleepiness; GTCS, generalized tonic–clonic seizure; HADS-D, Hospital Anxiety and Depression Scale-Depression subscale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety subscale; IGE, idiopathic generalized epilepsy; RLS, restless legs syndrome; SD, standard deviation.
[a] Sleep disturbances included symptoms of insomnia, obstructive sleep apnea, or restless legs syndrome.

**Table 3**
Logistic regression models for the factors associated with excessive daytime sleepiness in patients with epilepsy.

| | Total (n = 147) | | | Men (n = 73) | | | Women (n = 74) | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value |
| Employed | 4.469 | 1.571–12.715 | 0.005 | 6.771 | 1.299–35.283 | 0.023 | – | – | – |
| Having ≥1 sleep disturbance[a] | 3.626 | 1.576–8.344 | 0.002 | – | – | – | 3.661 | 1.188–11.281 | 0.024 |
| AED polytherapy | 2.663 | 1.143–6.202 | 0.023 | 2.998 | 0.903–9.949 | 0.073 | – | – | – |
| HADS-A scores | – | – | – | 1.164 | 1.005–1.349 | 0.043 | – | – | – |

Dependent variable = the presence or absence of excessive daytime sleepiness.
AED, antiepileptic drug; CI, confidence interval; HADS-A, Hospital Anxiety Depression Scale-Anxiety subscale; OR, odds ratio; SE, standard error.
[a] Sleep disturbances included symptoms of insomnia, obstructive sleep apnea, or restless legs syndrome.

## 4. Discussion

We determined factors contributing to EDS, which had a prevalence of 24.5% in the 147 Korean AWE in this study. Being employed, having at least one sleep disturbance, and taking AED polytherapy were independent factors related to EDS. However, significant sex differences were found: EDS was associated with being employed and anxiety in men but was associated with having at least one sleep disturbance in women. Depressive symptoms and other epilepsy-related variables were not statistically related to EDS.

In the literature, EDS, defined as an ESS score > 10, has been reported in 10% to 48% of AWE, compared with 0% to 18% of controls [7]. Some studies with a relatively lower prevalence of an ESS > 10 among controls (11% or less) reported that an ESS score > 10 was more common among AWE [10,12,22] whereas studies finding a prevalence greater than 11% in controls did not find a significantly higher prevalence in AWE [1,2,8,9]. In agreement with these findings, our previous study found a prevalence of EDS of 18.2% in healthy controls, a figure not significantly different than in AWE [15]. As noted above, such a situation suggests that EDS is attributable to factors shared in common by AWE and controls. One of such variable could be work hours. In 2017, Koreans had the third highest number of work hours among the 37 members of Organization for Economic Cooperation and Development [23]. A straw poll in 2016 suggested that Korean workers usually spend over 10 h a day on their jobs and only sleep for 6 h [24]. Such long working hours and sleep deprivation could result in EDS and consequently affect worker safety and health. The present study supports the importance of this factor, showing that employed AWE were more likely to have EDS than those who were unemployed. Subjective sleep quantity did not differ based on the presence or absence of EDS and employment.

Coexisting sleep disturbance was found to be the next most important factor contributing to EDS in our AWE. Adults with epilepsy with at least one sleep disturbance had about twofold higher prevalence of EDS than those without sleep disturbance (63.9% vs. 36.9%, OR: 3.626, $p < 0.01$). Our findings were in agreement with a recent systematic review that found that EDS (defined as an ESS score > 10) in epilepsy seems more often to be related to undiagnosed sleep disorders rather than to epilepsy-related factors [7,25].

In the present study, however, there was the significant sex difference in factors associated with EDS. Association between being employed and EDS was found but only in the subgroup of men with epilepsy. In contrast, coexisting sleep disturbance was associated with EDS but only in the subgroup of women with epilepsy. The reasons for the sex difference were unclear. With respect to the effects of being employed on EDS, however, possibilities included differences in work types and strength, work-related stress, and sleep deprivation. In the present study, subjective sleep quantity did not differ between men and women. There have been few studies regarding sex differences in factors associated with EDS in AWE. Therefore, relationships between EDS and the potential factors in AWE must be further evaluated based on sex.

The findings with regard to the effects of individual sleep disturbance on EDS in epilepsy have been inconsistent. In our study, OSA was assessed using the SA-SDQ but was not confirmed by polysomnography (PSG). Using the SA-SDQ with a cutoff of 29 for men and 26 for women suggested when studying AWE [20], both Khatami et al. [1] and we found a similar prevalence of OSA in AWE (30% and 23.1%, respectively). Weatherwax et al. [20] used the same SA-SDQ cutoff scores and found that it had sensitivities of 75% and 80% and specificities of 65% and 67%, respectively, for mild-to-severe OSA across all participants. Similar to our study, Khatami et al. [1] found no association between EDS and OSA in AWE, using the SA-SDQ. However, Malow et al. [9] found that EDS in AWE was associated with the severity of OSA, using a numeric variable derived from the SA-SDQ scores. Study findings in patients with epilepsy and OSA, as confirmed by PSG, were also inconsistent. In one study of 130 AWE, no association was found between EDS (defined as an ESS score > 9) and OSA (defined by apnea-hypopnea index ≥ 10 /h) [26]. In contrast, another study investigating OSA in AWE showed that EDS (defined as an ESS score > 10) was more frequent among individuals with OSA (23.1%), compared with individuals without OSA (9%) [27]. An association between RLS symptoms and EDS in patients with epilepsy was found in some studies [1,9] but not in our study or in other studies [8]. Given that having at least one sleep disturbance was significantly associated with EDS in epilepsy, low statistical power rather than a lack of statistical significance may be an explanation for inconsistent effects of individual sleep disturbances on EDS in epilepsy. The current study did not define sleep disorders using standard diagnostic criteria.

Other than AED polytherapy, we found no other epilepsy-related factors to be significantly related to EDS. Antiepileptic drug polytherapy did increase the risk, with EDS being more common in those taking more than one AED than in those on monotherapy. However, when the overall group was divided into the subgroups of men and women with epilepsy, each subgroup did not show such significant association; this was likely due to low statistical power, rather than a lack of statistical significance. Some longitudinal studies showed that daytime sleepiness decreased after a reduction of the number of AEDs [28,29]. In one study, both seizure frequency and OSA were predictors of EDS [8] while several others found no such association between EDS and epilepsy-related factors including the number of AEDs [1,7,9]. In spite of these findings, epilepsy-related factors should not be neglected as potential contributors to EDS in individual patients, as AEDs, seizures (both daytime and nocturnal), and the type of epilepsy have all been demonstrated to have an effect on sleep architecture [4,7,30,31]. A study of 130 outpatients with epilepsy found that AED load was one factor associated with OSA on multivariate analysis [26].

Both depression and anxiety are common psychiatric comorbidities in AWE and are well known to be associated with poor sleep quality and a high prevalence of insomnia [32]. Daytime sleepiness is a common feature of depression, and levels of daytime sleepiness have been found to indicate the severity of depressive symptoms [14]. Anxiety has also been cited as a factor associated with EDS [14]. However, there has been little research on associations between psychiatric comorbidities and daytime sleepiness in epilepsy. A Brazilian study found that anxiety measured by the Beck Anxiety Inventory (BAI) was linked to EDS in 99 unselected AWE [6]. In contrast, a Chinese study with 150 consecutive AWE recently reported no significant associations between ESS and depressive and anxiety symptoms measured using Beck Depression Inventory-II and BAI, respectively [33]. In the present study, EDS was significantly associated with a higher level of anxiety, as measured by HADS-A; however, this was solely in the subgroup of men with epilepsy on multivariate analysis. We believe that the high level of anxiety in our patients with insomnia symptoms could have led to insomnia, then to EDS.

To measure the degree of daytime sleepiness in clinical practice, the ESS and the multiple sleep latency test (MSLT) are commonly used methods. The MSLT is considered a gold standard objective measurement of tendency in falling asleep. In contrast, the ESS measures subjective sleep propensity [5]. The absence of a substantial correlation has been reported between ESS and MSLT results [34,35]. This suggests that the ESS and MSLT measure different aspects of sleepiness [35]. In our study, we measured daytime sleepiness subjectively using the ESS, but not objectively using the MSLT, which should be noted when interpreting the results of our study.

Our study had limitations and should be interpreted with some caution. First, sleep disturbances were assessed only subjectively by using questionnaires. Previously diagnosed sleep disorders and their treatment were not taken into consideration, and PSG was not performed. Furthermore, symptoms of insomnia and RLS were not assessed using established diagnostic criteria; therefore, the effects of specific sleep disorders on EDS could not be evaluated in this study. And we did not take into considerations our study population that was recruited from university hospitals, so that enrolled patients were likely to have more severe seizures than patients with epilepsy managed at primary care clinics. Moreover, we excluded a subset of AWE on the basis of our exclusion criteria. Therefore, some of our findings, such as the prevalence and severity of EDS, sleep disturbances, anxiety, and depression may not be applicable to other populations. Finally, we did not collect data on the number of patients who were excluded in this study. Therefore, we could not know how many patients were actually eliminated by the exclusion criteria.

In conclusion, subjective daytime sleepiness in AWE appears to have a multifactorial origin. Being employed, having sleep disturbance, and AED polytherapy were all independent predictors of EDS in Korean AWE. There may be sex differences in factors associated with EDS.

## Declarations of interest

None.

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