Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1503792

Subclinical seizures on EEG with sleep phases and clinical significance in patients with focal epilepsy

EEG'de uyku evresinde görülen subklinik nöbetler ve fokal epilepsili hastalarda klinik önemi

Çağla Erdoğan, İsmail Hakkı Akbudak, Ebru Apaydın Doğan

Posted date:24.06.2024 Acceptance date:09.12.2024

Abstract

Purpose: Studies have observed that subclinical seizures significantly impact diagnosis, prognosis, and treatment responses. The aim of our study is to investigate the presence of these seizures, their relationship with sleep, their contribution to diagnosis, and their impact on treatment selection and prognosis in patients diagnosed with partial epilepsy.

Materials and methods: A total of 1.626 EEGs conducted in the EEG unit were examined. Among them, 626 were found to belong to patients diagnosed with partial epilepsy. 140 patients who underwent twenty-minute EEG monitoring and 28 patients who underwent twenty-four-hour EEG monitoring were included in the study.

Results: A comparative analysis was conducted between two cohorts of patients: one subjected to a twenty-minute EEG and the other undergoing a 24-hour EEG. In the presence of resistant epilepsy, the risk of SCS is increased by 3.1 times. The presence of SCS in frontal lobe epilepsies demonstrated a 2.2-fold elevation compared to temporal lobe epilepsies (1.0-5.3). A statistically significant relationship between Levetiracetam usage and seizures was observed (p=0.044). The calculated Odds Ratio for risk indicated a 1.2-fold (1-1.6) higher frequency of seizures with Levetiracetam usage. Risk analysis revealed a 1.5%-fold (1.2-1.9) higher incidence of seizures with the use of well-known drugs in favor of lacosamide-zonisamide.

Conclusion: SCSs are gaining increasing clinical significance in terms of diagnosis, prognosis, and treatment. The relationship between these periods of sleep and SCSs is important for future research with a larger number of patients and medical professionals.

Keywords: Subclinical seizures, sleep, focal epilepsy.

Erdogan C, Akbudak IH, Apaydin Dogan E. Subclinical seizures on EEG with sleep phases and clinical significance in patients with focal epilepsy. Pam Med J 2025;18:282-292.

Öz

Amaç: Çalışmalarda, subklinik nöbetlerin tanı, prognoz ve tedavi yanıtları üzerinde önemli bir etkisi olduğu gözlemlenmektedir. Çalışmamızın amacı, parsiyel epilepsi tanısı konmuş hastalarda bu nöbetlerin varlığını araştırmak, uyku ile ilişkilerini incelemek, tanıya katkılarını ve tedavi seçimi ile prognoz üzerindeki etkilerini değerlendirmektir.

Materyal ve yöntem: EEG ünitesinde yapılan toplam 1,626 EEG incelendi. Bunların içinde, parsiyel epilepsi tanısı konmuş 626 hastaya ait EEG bulundu. Çalışmaya yirmi dakika EEG monitörizasyonu yapılan 140 hasta ve yirmi dört saat EEG monitörizasyonu yapılan 28 hasta dahil edildi.

Bulgular: İki hasta grubu arasında karşılaştırmalı bir analiz yapıldı: biri yirmi dakika EEG'ye tabi tutulan diğeri 24 saat EEG monitörizasyonu yapılan. Dirençli epilepsi varlığında, SCS riski 3.1 kat artmaktadır. Frontal lob epilepsilerinde SCS varlığı, temporal lob epilepsilere kıyasla 2.2 kat daha yüksek bulundu (1,0-5,3). Levetirasetam kullanımı ile nöbetler arasında istatistiksel olarak anlamlı bir ilişki gözlemlendi (p=0,044). Risk oranı hesaplaması, Levetirasetam kullanımı ile nöbetlerin 1.2 kat (1-1,6) daha sık oluşma olasılığını gösterdi. Risk analizi, lakozamid-zonisamid gibi bilinen ilaçların kullanımı lehine nöbetlerin %1,5 kat (1,2-1,9) daha sık görüldüğünü ortaya koydu.

Sonuç: Subklinik nöbetler, tanı, prognoz ve tedavi açısından giderek artan klinik öneme sahiptir. Bu nöbetlerin uyku ile ilişkisi, daha geniş hasta ve merkezlerle yapılacak gelecek araştırmalar için önem taşımaktadır.

Anahtar kelimeler: Subklinik nöbetler, uyku, fokal epilepsi.

Erdoğan Ç, Akbudak İH, Apaydın Doğan E. EEG'de uyku evresinde görülen subklinik nöbetler ve fokal epilepsili hastalarda klinik önemi. Pam Tıp Derg 2025;18:282-292.

Çağla Erdoğan, Ph.D. Pamukkale University, Medicine Faculty, Intensive Care Department, Denizli, Türkiye, e-mail: caglaerdogan89@gmail.com (https://orcid.org/0000-0001-8772-6565) (Corresponding Author)

İsmail Hakkı Akbudak, Assoc. Prof. Pamukkale University, Medicine Faculty, Intensive Care Department, Denizli, Türkiye, e-mail: ishakbudak@gmail.com (https://orcid.org/0000-0002-3716-9243)

Ebru Apaydın Doğan, Prof. Akdeniz University, Medicine Faculty, Neurology Department, Antalya, Türkiye, e-mail: eapaydindogan@yahoo.com (https://orcid.org/0000-0002-6818-3021)

Introduction

The electroencephalography (EEG) examinations conducted on patients with epilepsy reveal various patterns related to pathologies. Sharp waves, spike waves, and spike-wave complexes are identified among these pathologies. Numerous studies exist regarding both the characteristics and clinical significance of these patterns. However, the clinical significance of subclinical seizures is not clearly defined. Subclinical seizures (SCS) are defined as electrographic seizures consisting of rhythmic ictal discharges that do not lead to objective or subjective changes in consciousness or behavior and are spread over time. SCS can be detected through intracranial or surface EEG monitoring. In many studies, data suggest that SCS originating from the same cortical area as clinical seizures can be used for diagnosis by determining the epileptogenic area [1].

There are few studies on SCS. Although the exact prevalence of SCS is unknown, a study by Velkey et al. [2] found a subclinical seizure rate of 18% in long-term EEG monitoring in children, contributing to the diagnostic process by 85%. When reviewing the literature, it is indicated that SCS can be used for surgical prognosis and predictions of seizure freedom [3]. In a study by Fernandez Torré et al. [4], the presence of SCS in patients with glioma is reported as a sign in favor of progression. Evidence also suggests that SCS may be associated with memory deficits and autonomic dysfunction. Vossel et al. [5] investigated the presence of SCS in patients followed up with a diagnosis of Alzheimer's disease. SCS was detected in 42% of the patients, and when these patients were followed up, it was observed that cognition and executive functions were lost faster in patients with SCS. 60% of the identified SCS occurred during sleep.

Jin et al. [6] conducted studies on the prevalence and characteristics of SCS. In these studies, the presence of these seizures was found to be associated with pharmacoresistant epilepsy and abnormal MRI. The prevalence was found to be 5.3%, and it was stated that SCS provided information about the localization of the epileptogenic focus in 79.4% of the patients with SCS. It was reported that 7.7% of these seizures were detected in a 20-minute EEG, 83.3% in a 24-hour EEG, and 92.8% in a 48-hour EEG. Most of these seizures were detected during sleep.

In a recent study, a significant increase in the risk of seizures was found in the presence of epileptiform discharges detected in EEG. It was suggested that subclinical and clinical seizure patterns have similar circadian rhythms and are formed by the same regulatory mechanisms. Studies have suggested that SCS can cause permanent neuronal changes and may lead to cognitive defects that could result in sequelae. For this reason, many authors believe that SCS requires treatment in the same way as clinical seizures. Anderson et al. [7] examined the circadian pattern of SCS. It was determined to be most common between 23:00 and 05:00. Investigating SCS during sleep is considered effective in understanding clinical treatment responses and selecting the most appropriate treatment time.

It is observed that SCS have a significant impact on the diagnosis, prognosis, and treatment responses. In our clinic, we plan to investigate the presence of these seizures, their relationship with sleep, their contribution to diagnosis, and their impact on treatment selection and prognosis in patients diagnosed with focal epilepsy.

Material and methods

Patients who applied to our clinic and underwent monitoring in the EEG unit within the last year were included in the study. Retrospectively, the demographic information of the patients, details of the disease diagnosis and treatment, and the presence of resistant epilepsy were scanned through the hospital information management system. Patients with focal epilepsy who underwent EEG monitoring and had pathological changes in their EEG were included in the study.

Permission was obtained from the Akdeniz University Clinical Research Ethics Committee for the study (permission date: 13/07/2017 and permission number: 70904504/258).

EEG monitoring

EEG monitoring was conducted using surface electrodes placed according to the international 10-20 system and VEEG digital systems.

Routine 20-minute EEG monitoring sessions and 24-hour EEG monitoring sessions performed on the presenting patients were considered for analysis. This study aimed to investigate the detection rate and clinical significance of subclinical seizures (SCSs) and sleep through routine EEG monitoring. For this reason, short EEG monitoring sessions were also included in the study. In statistical analyses, short-term and 24-hour EEG monitoring sessions were evaluated separately and, ultimately, together.

The presence of sleep in the conducted EEGs was assessed according to the EEG patterns defined in the literature based on the American Academy of Sleep Medicine (AASM) scoring system for sleep stages.

The presence of SCSs in EEGs and its relationship with sleep were examined. Whether SCSs were observed during wakefulness or sleep, and if observed during sleep, in which stage they occurred.

A total of 1.626 EEGs conducted in the EEG unit were examined. Ninety-six of these EEGs had a duration of twenty-four hours. Among them, 626 were found to belong to patients diagnosed with focal epilepsy. After being evaluated by two independent EEG specialists, these EEGs were scrutinised, with a joint decision that those exhibiting focal epileptiform features were included in the study. As a result, a total of 140 patients who underwent twenty-minute EEG monitoring and 28 patients who underwent twenty-four-hour EEG monitoring were included in the study.

Subclinical seizure definition

SCSs (Subclinical Seizures) are defined as paroxysmal rhythmic epileptiform EEG patterns that spread over time and localization without subjective or objective clinical findings. The absence of alpha rhythm in wakefulness, posterior reactive rhythm, and focal or generalized slowing are considered abnormal. The absence of age-appropriate sleep spindles, the presence of asymmetric sleep spindles, and continuous asynchrony are considered abnormal during sleep. Electrographic seizure is defined as rhythmic epileptiform activity lasting longer than 10 seconds, not giving rise to clinical symptoms but showing development over time and space, even causing changes in connected electrodes [3].

During video EEG monitoring, patients' subjective complaints are questioned and objectively monitored for seizures. Electrographic seizures without any clinical signs are considered subclinical seizures (SCSs).

Statistical analysis

Statistical analysis was conducted utilizing SPSS 18 Software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were applied to summarize continuous data, expressing them as the median with the range and mean with standard deviation (mean±SD). Categorical data were presented in terms of numbers and percentages. The Chi-square test was used to compare categorical variables, and a significance test for the difference between two means was employed to compare continuous variables. For variables with significant results in the Chi-square test, Odds Ratio (OR) was calculated. A significance level of $p<0.05$ was considered.

Results

Of the patients who underwent a twenty-minute EEG, 56.4% were female, and 43.6% were male. The patients who underwent a twenty-minute EEG ranged from 17 to 89 years old. Their average age was calculated as 42.5±19.9. It was determined that 22.1% of the participants have resistant epilepsy, 33.6% have the presence of sleep in their EEG, and when EEGs with sleep were examined, 60.6% of the seizures occurred in the NREM-1 stage. Additionally, 37.1% of the patients were found to have a frontal lobe epilepsy focus. The patients who underwent a twenty-minute EEG ranged from 17 to 89 years old. Their average age was calculated as 42.5±19.9. The duration of illness varies between 1 and 45 years, with an average of 8.3±10.1 years (Table 1).

Among the cohort subjected to a twenty-four-hour EEG, 67.9% were of the female gender, while 32.1% were male. Notably, 53.6% of the participants had resistant epilepsy. When examining the presence of subclinical seizures (SCS) during sleep, researchers found that 3.6% of seizures occurred in the light sleep stage (NREM-1), while 96.4% occurred during deep sleep. A predominant frontal lobe epilepsy focus was discerned in 60.7% of the patients. The age range of individuals undergoing the EEG protocol ranged from 18 to 67 years, with an average age of 33.9±12.7. Regarding the duration of illness, a variance between 1 and 39 years was noted, with an average duration of 11.21±10.5 years (Table 1).

Table 1. Distribution of demographic and clinical characteristics of patients

Parameters	20 Minutes EEG Group	24-Hour EEG Group
Gender Distribution	Female: 79 (56.4%)	Female: 19 (67.9%)
	Male: 61 (43.6%)	Male:9 (32.1%)
Age (Mean)	42.5	33.9
Refractory Epilepsy	31 (22.1%)	13 (53.6%)
Presence of Sleep in EEG	93 (66.4%)	28 (100%)
Presence of SCS in Sleep	66 (47.1%)	28 (100%)
Stages of Sleep for SCS	NREM-1: 40 (60.4%)	NREM-1: 1 (3.6%)
	NREM-2: 26 (39.4%)	NREM-2/3: 27 (96.4%)
Epileptic Focus	Frontal: 52 (37.1%)	Frontal: 17 (60.7%)
	Temporal: 60 (42.9%)	Temporal: 9 (32.1%)
		Other: 2 (7.1%)
Disease Duration (Mean)	8.3 year	11.21 year

When looking at medication use in patients who had a 20-minute EEG, it was found that 14% were not taking any medication. Notably, 40% were on monotherapy, while those employing five medications comprised a mere 2%. Upon examination of the pharmacological profiles of patients subjected to a twenty-four-hour EEG, it was observed that 18% refrained from using any medication. Additionally, 36% were noted to be utilizing a singular medication, with the highest medication usage capped at three, constituting 21% of the patient cohort (Table 2).

When examining the pharmaceutical usage among 168 patients in terms of both numerical counts and percentages, levetiracetam emerged as the predominant medication with a utilization rate of 50%. Subsequently, zonisamide followed with a utilization rate of 17.9%, oxcarbazepine with 14.9%, and lacosamide also with 14.9%. Phenytoin constituted a 3% usage rate, while phenobarbital concluded the list with a usage rate of 1.8% (Table 2).

Table 2. Data related to the treatment of patients

Parameters	Value
Number of Medications	
20 Minutes EEG group	
No medication	14%
1	49%
2	19%
3	12%
4	4%
5	2%
24 Hour EEG Group	
0	18%
1	36%
2	25%
3	21%
Medications	
Levetiracetam	84 (50%)
Zonisamide	30 (17.9%)
Oxcarbazepine	25 (14.9%)
Lacosamide	25 (14.9%)
Carbamazepine	23 (13.7%)
Valproate	22 (13%)
Lamotrigine	20 (11.9%)
Topiramate	8 (4.8%)
Phenytoin	5 (3%)
Phenobarbital	3 (1.8%)

In the cohort undergoing a twenty-minute EEG, an analysis was conducted on the relationships between the presence of SCS in sleep and gender, the number of medications used, the presence of refractory epilepsy, and the epileptic focus. A statistically significant association was identified solely between the presence of SCS and the epileptic focus (p=0.004) (Table 3).

A comparative analysis was conducted between two cohorts of patients: one subjected to a twenty-minute Electroencephalogram (EEG) and the other undergoing a 24-hour EEG. The former group is denoted as Group 1. In Group 1, 56.4% of subjects were female, contrasting with 67.9% in Group 2. No statistically significant distinction in gender distribution was discerned between the two cohorts (p=0.263). Upon comparing the two cohorts, a similar prevalence of singular drug usage was observed. Specifically, 49.3% in Group 1 and 35.7% in Group 2 reported single-drug administration. No statistically significant variance in drug utilization was identified between the groups (p=0.432) (Table 4).

Resistant epilepsy was diagnosed in 22.1% of Group 1 and 46.4% of Group 2, revealing a noteworthy statistical discrepancy (p=0.004). Notably, the incidence of resistant epilepsy was markedly higher in subjects undergoing a 24-hour EEG. In evaluating sleep stages between the two groups, it was noted that 60.6% of Group 1 SCSs manifested during Non-Rapid Eye Movement Stage 1 (NREM1), while 96.4% of Group 2 exhibited SCSs during NREM2 and NREM3 stages. A statistically significant disparity was evident between the two cohorts (p=0.0001) (Table 4).

Concerning the comparative assessment of epileptic foci, patients with frontal lobe epilepsy comprised 37.1% in Group 1 and 60.7% in Group 2, whereas those with temporal lobe epilepsy constituted 42.9% in Group 1 and 32.1% in Group 2. A statistically significant distinction was observed between the two groups (p=0.005). An OR analysis was employed to ascertain the risk in subjects exhibiting SCS and significant statistical differences. In the presence of resistant epilepsy, the risk of SCS is increased by 3.1 times (1.3-7.08). Furthermore, the presence of SCS during NREM2 and NREM3 stages exhibited a 41.5-fold increase compared to NREM1 (5.3-324.6). Lastly, the presence of SCS in frontal lobe epilepsies demonstrated a 2.2-fold elevation compared to temporal lobe epilepsies (1.0-5.3) (Table 4).

An examination was conducted on the relationship between the presence of Levetiracetam, the most-used medication in the groups, and subclinical seizures. Levetiracetam usage was identified in 56.4% of patients with subclinical seizures. A statistically significant relationship between Levetiracetam usage and seizures was observed (p=0.044). The calculated OR for risk indicated a 1.2-fold (1-1.6) higher frequency of seizures with Levetiracetam usage (Table 5).

Table 3. The relationship between the presence of SCS in sleep and other parameters in the 20-minute EEG cohort

	No SCS in Sleep		Presence of SCS in Sleep		
Parameters	**Number of patients**	**Percent of patients (%)**	**Number of patients**	**Percent of patients (%)**	***p*-value**
Gender					
Female	42	56.8	37	56.1	0.953
Male	32	43.2	29	43.9	X^2:0.007[a]
Total	74	100	66	100	
Number of Medication					
0	6	8.1	14	21.2	
1	39	52.7	30	45.5	
2	16	21.6	11	16.7	0.355
3	8	10.8	8	12.1	X^2:5.527[a]
4	4	5.4	2	3	
5	1	1.4	1	1.5	
Total	74	100	66	100	
Refractory Epilepsy					
Yes	17	23	14	21.2	0.482
No	57	77	52	78.8	X^2:0.063[a]
Total	74	100	66	100	
Epileptic Focus					
Frontal	18	24.3	34	51.5	0.004*
Temporal	38	51.4	22	33.3	X^2:11.054[a]
Others	18	24.3	10	15.2	
Total	74	100	66	100	

[a]Pearson Chi-Square Test, *:p<0.05 statistically significant

Table 4. Comparison of the demographic and clinical characteristics of patient groups undergoing twenty minutes and twenty-four hours of EEG

	Group 1		Group 2				
	Number	**Percent**	**Number**	**Percent**	***p*-value**	**OR**	**CI-Confidence Interval**
Gender							
Female	79	56.4	19	67.9	0.263	-	
Male	61	43.6	9	32.1	X^2:1.254[a]		
Number of Medication							
0	20	14.3	5	17.9			
1	69	49.3	10	35.7			
2	27	19.3	7	25	0.432		
3	16	11.4	6	21.4	X^2:4.872[a]	-	
4	6	4.3	0	0			
5	2	1.4	0	0			
Refractory Epilepsy							
Yes	31	22.1	13	46.4	0.004*		
No	109	77.9	15	53.6	X^2:7.119[a]	3.1	(1.3-7.08)
Sleep Stage							
NREM1	40	60.6	1	3.6	0.0001*		
NREM2+3	26	39.4	27	96.4	X^2:65.61[a]	41.5	(5.3-324.6)
Epileptic Focus							
Frontal	52	37.1	17	60.7			
Temporal	60	42.9	9	32.1	0.05* X^2:5.969[a]	2.2	(1.0-5.3)
Others	28	20	2	7.1			

[a]Pearson Chi-Square Test, *:p<0.05 statistically significant

Table 5. The relationship between Levetiracetam usage and subclinical seizures

Levetiracetam Usage	**Subclinical Seizures**				***p*-value**
	No		**Yes**		
	Number	**Percent**	**Number**	**Percent**	
Yes	31	41.9	53	56.4	0.044* X^2:3.47[a]
No	43	58.1	41	43.6	
Total	74	100	94	100	

[a]Pearson Chi-Square Test OR:1.2 (CI-confidence interval: 1-1.6), *:p<0.05 statistically significant

The relationship between the long-standing use of well-known anti-seizure medications and the new-generation anti-seizure treatments with seizures has been investigated in the groups. Patients using Levetiracetam, valproate, oxcarbazepine, and carbamazepine (Group 1) were compared with those using lacosamide and zonisamide (Group 2). Among patients experiencing subclinical seizures, 34% were using Group 1 drugs, while in those without subclinical seizures, this percentage was found to be 13.5%. A significant statistical difference was observed between the two groups (p=0.002). Risk analysis revealed a 1.5-fold (1.2-1.9) higher incidence of seizures with the use of Group 1 drugs (Table 6).

Table 6. The relationship between the usage of medications in Group 1 and Group 2 and seizures

	Subclinical Seizures				
	No		Yes		*p*-value
	Number	Percent	Number	Percent	
Group 1	10	13.5	32	34	0.002* X^2:9.3[a]
Group 2	64	86.5	62	66	
Total	74	100	94	100	

[a]Pearson Chi-Square Test OR: 1.5 (CI-confidence interval:1.2-1.9), *:p<0.05 statistically significant

Discussion

In the preliminary findings of our clinical study, it has been observed that sleep patterns can be detected even in the twenty-minute EEG monitoring of patients presenting to the outpatient clinic. The more frequent detection of SCSs during sleep also assists in capturing foci.

In our study, 1626 EEGs were examined. Of these, 626 belonged to patients diagnosed with focal epilepsy (38.4%). When looking at the presence of subclinical seizures in these EEGs, it was observed that a total of 168 showed epileptiform changes. This figure represents 10.3% of all EEGs, in line with other studies described below, and 26.8% of patients diagnosed with focal epilepsy. Our clinic is an advanced treatment centre that follows up on refractory epilepsy and offers surgical treatment options. Consequently, subclinical seizures are observed more frequently in our examinations.

A recent study examined the presence of subclinical seizures in stereotactic EEG. Subclinical seizures were detected in 84 out of 164 patients, indicating a high rate of around 50%. Although the surface electrodes we routinely use do not detect at such high rates, the detection percentage increases in the presence of appropriate indications and refractory epilepsy. Since our patients fit these conditions, the presence of subclinical seizures is detected at a higher rate [8].

There is limited research on the clinical and treatment-related data of SCSs, and their prevalence is not well-known. In a study by Velkey et al. [2], the observed rate of SCSs in long-term EEG monitoring in children was 18%, and their contribution to the diagnostic process was determined to be 85%. There is also a study utilizing positron emission tomography (PET) in the presence of SCSs, demonstrating the detection of the focus and pathology [9].

Jin et al. [6] have conducted studies on the prevalence and characteristics of SCSs. In these studies, the presence of these seizures has been found to be associated with pharmacoresistant epilepsy and abnormal MRI. The prevalence was determined to be 5.3%, and it has been noted that the presence of SCSs provides information on epileptogenic focus localization in 79.4% of patients. It was indicated that 7.7% of SCSs were detected in 20-minute EEG, 83.3% in 24-hour EEG, and 92.8% in 48-hour EEG. The majority of these seizures were observed during sleep.

In our study, the presence of sleep was detected in 66% of patients who underwent a twenty-minute EEG, and 47% of these individuals exhibited SCSs. In patients undergoing 24-hour EEG monitoring, all of them displayed sleep patterns, and SCSs were identified in 100% of these cases. All seizures that were observed occurred during sleep. Given that polysomnography and electrooculography were not used, differentiation of the REM phase was not considered in the assessment.

NREM2 and NREM3 stages were collectively considered as deeper sleep stages than NREM1. A significant association was found between sleep staging and SCS, with a noticeable increase in risk favoring deep sleep. Due to the small number of patients, an OR of 41 was determined. The occurrence of SCS during surface sleep in a patient undergoing 24-hour EEG monitoring may have contributed to this result. It is believed that with an increase in the number of patients, this ratio will be more normalized. The higher risk associated with deep sleep aligns with findings in other studies [10].

In the study by Farooque and Duckrow [3], SCSs in patients who underwent epilepsy surgery were considered. The results indicated that 64% of patients showing the presence of SCSs in the area where epilepsy surgery was performed had a favorable prognosis. It was suggested that SCSs could be used for predicting surgical prognosis and non-seizure follow-ups. In the same study, it was shown that SCSs in the included patients mostly originated from outside the temporal region, although in many other studies, they were predominantly thought to be temporal in origin [1].

In patients subjected to a twenty-minute EEG, a temporal focus was identified in 42% of cases, while a frontal focus was noted in 37%. Among those who underwent a 24-hour EEG, a frontal focus was detected in 60% of cases. This result, which differs from other studies, is thought to be related to patient selection. Patients with detected frontal and temporal foci had previously received these diagnoses and are being followed up accordingly.

Advanced statistical analyses revealed that the presence of SCS was 2.2 times more likely in individuals with a frontal focus compared to those with a temporal focus. The risk of experiencing SCSs during sleep was found to be elevated in patients with frontal lobe epilepsy. This heightened risk was consistently observed in both short-term and long-term EEG recordings. This observation suggests that the probability of diagnosing frontal lobe epilepsy increases when patients are induced into sleep during short-term EEG recordings.

Reducing the frequency and severity of epileptic attacks leads to a noticeable improvement in clinical outcomes. Various studies have shown that patients with SCS have decreased in memory and cognitive functions. There is evidence supporting the notion that SCSs contribute to memory impairment and autonomic dysfunction [9-13]. The treatment and elimination of SCSs have been associated with a significant improvement in cognitive functions in these cases [11, 14, 15].

In the study conducted by Vossel et al. [5] on patients diagnosed with Alzheimer's disease (AD), SCSs were identified in 42.2% of patients with AD. At the time SCSs were detected, there were no clinical symptoms present in the patients. However, follow-up observations have shown that patients with SCSs experience a faster cognitive decline process.

To assess the relationship between the treatment process of SCSs and medications, the study included data on the number and types of medications used by patients. Analysis of medication usage revealed a higher prevalence of monotherapy in patients undergoing short-term EEG. The use of more than three medications was similarly observed in this group. Upon closer examination of these patients, it was noted that all of them were in a medication transition phase. In contrast, many of the patients who underwent 24-hour EEG were potential candidates for epilepsy surgery, and their medications were more consistently regulated and monitored. As a result, a more even distribution of medication numbers was observed. While no significant difference was found between the number of medications and SCSs, the proximity to statistical significance suggests that with an increase in the number of patients, this relationship could gain significance.

Therefore, the study suggests that polytherapy may be favorable in patients with SCSs. It was observed that 50% of the patients in the study used levetiracetam. The high prevalence of levetiracetam usage was attributed to the difficulty in distinguishing between focal epilepsy and generalized epilepsy, leading to a broad spectrum of medication choices. Consequently, when examining the OR in patients using levetiracetam, a 1.2-fold increase in the risk of SCSs was observed. This finding underscores the importance of meticulous diagnosis of focal epilepsy and suggests that medication selection based on this diagnosis may be more effective in seizure control.

In recent years, new treatment options have emerged in the battle against epilepsy. Among these, the most preferred ones are lacosamide and zonisamide. The study indicates a high utilization rate of 17.9% and 14.9% for these two drugs among the patients. The effectiveness of these two drugs was compared with others. In the comparison between patients using frequently preferred drugs in neurology clinics (levetiracetam, valproate, oxcarbazepine, and carbamazepine) and those using newer-generation drugs, a significant statistical difference was observed. In patients using four

drugs, a 1.5-fold increase in the risk of SCS was detected according to the calculated OR. Increasing the number of patients could allow for a more detailed analysis of this comparison, potentially revealing more substantial differences.

The reason for categorizing patients into two groups lies in the absence of 24-hour EEG recording facilities in many centres. This underscores the need to demonstrate whether meaningful findings can be detected with short-term EEG. In most short-term EEG recordings, a sleep pattern is evident, and most seizures are detected during sleep stages. This suggests that the probability of detecting epileptiform changes in EEGs recorded with patients being induced into sleep is higher, providing us with an easier diagnostic opportunity. Even in a twenty-minute EEG recording, the presence of characteristics of NREM1 and NREM2 stages is valuable when considering the relationship between SCS and sleep.

In patients presenting with suspicion of epileptic seizures, a diagnosis of focal or generalized epilepsy should be meticulously established, and appropriate medication selection should be made. The study indicates that broad-spectrum anti-seizure treatment options are less effective compared to newer-generation medications, with a particular increase in risk noted for levetiracetam.

Regarding the limitations of our study, it is thought that the small number of patients who underwent 24-hour EEG may cause the statistical risk ratio to be overestimated. Studies with larger sample sizes need to be planned for more consistent responses. It was observed that many of the patients who underwent 24-hour EEG were followed up because they were diagnosed with resistant epilepsy or were planned for surgery. Due to this situation, a significant difference was observed in the number of medications between the two groups.

Sleep serves as one of our tools in examining both physiological and pathological events. It is utilized to reveal underlying pathologies that may not be apparent. SCSs are gaining increasing clinical significance in terms of diagnosis, prognosis, and treatment. The relationship between these two aspects holds importance for future research with a larger number of patients and centres.

Funding: None.

Authors contributions: C.E., E.A.D. have constructed the main idea and hypothesis of the study. C.E., E.A.D. developed the theory and arranged the material and method section. C.E., E.A.D. have done the evaluation of the data in the Results section. The Discussion section of the article was written by C.E. C.E., E.A.D., İ.H.A. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Zangaladze A, Nei M, Liporace JD, Sperling MR. Characteristics and clinical significance of subclinical seizures. *Epilepsia*. 2008;49(12):2016-2021. doi:10.1111/j.1528-1167.2008.01672.x
2. Velkey A, Siegler Z, Janszky J, Duray B, Fogarasi A. Clinical value of subclinical seizures in children with focal epilepsy. *Epilepsy Res*. 2011;95(1-2):82-85. doi:10.1016/j.eplepsyres.2011.03.001
3. Farooque P, Duckrow R. Subclinical seizures during intracranial EEG recording: are they clinically significant?. *Epilepsy Res*. 2014;108(10):1790-1796. doi:10.1016/j.eplepsyres.2014.09.020
4. Fernández Torre JL, Hernández Hernández M, Martino J, Hinojo C. Subclinical focal seizures as a sign of progression in gliomas. *Epileptic Disord*. 2014;16(4):546-553. doi:10.1684/epd.2014.0701
5. Vossel KA, Ranasinghe KG, Beagle AJ, et al. Incidence and impact of subclinical epileptiform activity in Alzheimer's disease. *Ann Neurol*. 2016;80(6):858-870. doi:10.1002/ana.24794
6. Jin B, Wang S, Yang L, et al. Prevalence and predictors of subclinical seizures during scalp video-EEG monitoring in patients with epilepsy. *Int J Neurosci*. 2017;127(8):651-658. doi:10.1080/00207454.2016.1220946
7. Anderson CT, Tcheng TK, Sun FT, Morrell MJ. Day-Night Patterns of Epileptiform Activity in 65 Patients With Long-Term Ambulatory Electrocorticography. *J Clin Neurophysiol.* 2015;32(5):406-412. doi:10.1097/WNP.0000000000000183
8. Cox BC, Khattak JF, Starnes K, et al. Subclinical seizures on stereotactic EEG: characteristics and prognostic value. *Seizure*. 2022;101:96-102. doi:10.1016/j.seizure.2022.07.015

9. la Fougère C, Rominger A, Förster S, Geisler J, Bartenstein P. PET and SPECT in epilepsy: a critical review. *Epilepsy Behav*. 2009;15(1):50-55. doi:10.1016/j.yebeh.2009.02.025
10. Frauscher B, Gotman J. Sleep, oscillations, interictal discharges, and seizures in human focal epilepsy. *Neurobiol Dis*. 2019;127:545-553. doi:10.1016/j.nbd.2019.04.007
11. Brotherstone R, McLellan A. Parasympathetic alteration during sub-clinical seizures. *Seizure*. 2012;21(5):391-398. doi:10.1016/j.seizure.2012.03.011
12. Akman CI, Montenegro MA, Jacob S, et al. Subclinical seizures in children diagnosed with localization-related epilepsy: clinical and EEG characteristics. *Epilepsy Behav*. 2009;16(1):86-98. doi:10.1016/j.yebeh.2009.06.026
13. Adjei P, Surges R, Scott CA, Kallis C, Shorvon S, Walker MC. Do subclinical electrographic seizure patterns affect heart rate and its variability?. *Epilepsy Res*. 2009;87(2-3):281-285. doi:10.1016/j.eplepsyres.2009.08.011
14. Puteikis K, Wolf P, Mameniškienė R. Longer-term verbal and visual memory patterns in patients with temporal lobe and genetic generalized epilepsies. *Epilepsia Open*. 2023;8(4):1279-1287. doi:10.1002/epi4.12779
15. Kanazawa K, Matsumoto R, Shimotake A, et al. Persistent frequent subclinical seizures and memory impairment after clinical remission in smoldering limbic encephalitis. *Epileptic Disord*. 2014;16(3):312-317. doi:10.1684/epd.2014.0664