



## Epilepsy and headaches: Further evidence of a link<sup>☆</sup>



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### ABSTRACT

**Objective:** Epilepsy and primary headaches are two of the most common neurologic conditions that share some common clinical characteristics, and can affect individuals of all age groups around the world. In recent years, the underlying pathophysiologic mechanisms potentially common to both headaches and epileptic seizures have been the subject of scrutiny. The objective of this study was to determine the frequencies and types of headaches in patients with epilepsy, and evaluate any temporal relationship with epileptic seizures.

**Method:** Demographic data, epilepsy durations, seizure frequencies, seizure types and antiepileptic medications used were captured of 349 patients who were followed up at our epilepsy outpatient clinic. Patients who experienced headaches were grouped based on the type of headaches and on whether their headaches occurred in the preictal, postictal or interictal period.

**Result:** Three hundred forty-nine patients (190 females, 159 males) were enrolled in the study. The patients' average age was  $30.9 \pm 13.1$  years, and average epilepsy duration was  $13.5 \pm 10.9$  years. The types of epileptic seizures were partial in 19.8% of patients, generalized in 57.9%, and secondary generalized in 20.3% of patients. Some 43.6% of the patients did not experience headaches, and 26.9% had migraine and 17.2% tension-type headaches. Headaches could not be classified in 12.3% of patients. The headaches occurred preictally in 9.6%, postictally in 41.6% and interictally in 8.6% of patients. The ratio of headaches was lower in male patients compared with females, and females experienced migraine-type headaches more frequently compared with males ( $p=0.006$ ). Migraine-type headaches were less frequent among patients who experienced less than one seizure per year, but more frequent ( $p=0.017$ ) among those who experienced more than one seizure per month, but less than one seizure per week. Migraine-type headaches were significantly more frequent ( $p=0.015$ ) among patients receiving polytherapy compared with patients receiving monotherapy.

**Conclusion:** The results of this study suggest that headaches, particularly migraine-type headaches, were frequently experienced by patients with epilepsy, postictal headaches were more common, and the frequency of migraine attacks could be linked with seizure frequency and the type of treatment.

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### 1. Introduction

Epilepsy and primary headaches are two of the most common neurologic conditions. They share some clinical characteristics and can affect individuals of all ages around the world. Both conditions originate from neuronal hyperexcitability, and both result in episodes of neurologic dysfunction. In the general population, the prevalence of lifelong headaches is 46% and the prevalence of migraine is between 10 and 22% [1–3], although the reported prevalence of active epilepsy is 0.3–0.7% [1,4].

The association of headaches and epilepsy is well-known. It has been reported that the frequency of epilepsy in patients with migraine (1–17%) is higher than the frequency of epilepsy in the general

population (0.5–1%). Moreover, the prevalence of migraine is higher among patients with epilepsy (8–23%) compared to healthy individuals [1,5,6]. Co-occurrence of migraine and epilepsy in the same patient can have three interpretations: 1) both migraine and epilepsy are common in the population and therefore may coexist in the same individual; 2) migraine and epilepsy share common underlying pathophysiologic and/or genetic causes; and 3) both conditions are causally related and one may lead to the other in some patients [7].

In recent years, pathophysiologic mechanisms that can occur in both headaches and epileptic seizures have been the subject of study. The pathogenesis of both conditions include the modification of membrane channel functions and the imbalance of excitatory and inhibitory factors [8]. Most studies support the hypothesis that increased neocortical cellular excitability is the main underlying mechanism for both migraine and epileptic seizures [7]. It has been suggested that hyperexcitability facilitates the transition to cortical spreading depression (CSD) in migraine, causing hypersynchronous activity in epilepsy. Cortical spreading depression is considered to be an underlying factor in the

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pathophysiology of migraine and epilepsy. In CSD and the epileptic focus, onset and propagation occur when neurologic events reach a certain threshold. It has been proposed that CSD and epileptic seizures can trigger the onset of one another [7,9]. In both conditions, depolarization and hypersynchronization can occur through multiple pathways. In a migraine attack or epileptic seizure, the hyperexcitation of epilepsy occurs as a result of a paroxysmal change in the cortical neuronal activity, whereas in migraine, hypoexcitation and hyperexcitation, respectively, occur as a rebound phenomenon [7].

CSD reduces the triggering threshold of the epileptic focus, which increases the risk of seizures following a preictal headache [8]. However, the threshold of CSD is lower than that required for an epileptic seizure, which is why migralepsy is quite uncommon. On the other hand, recurring seizures cause CSD in the patient, which may increase the risk of preictal headaches and may also be associated with more frequent postictal headaches versus preictal and ictal headaches in patients with epilepsy [7,9–11].

The objective of this study was to determine the frequency and types of headache in patients with epilepsy, and evaluate any temporal relationship with epileptic seizures.

## 2. Method

Three hundred forty-nine patients who were followed at the Epilepsy Outpatient Clinic of the Neurology Ward at Dışkapı Yıldırım Beyazıt Education and Research Hospital were consecutively enrolled in the study. Patients  $\geq 17$  years with the ability to answer the questionnaire were invited to participate in the study. Patients were interviewed by using a standard questionnaire to determine if their epileptic seizures and headaches occurred independently or if headaches occurred in a temporal relationship to the seizures. Patients who had experienced at least 2 unprovoked seizures and had been followed for epilepsy for a minimum of 2 years were included in the study. The diagnoses of migraine and tension-type headache (TTH) were made based on International Classification of Headache Disorders (IHSS III-beta) criteria. Patients in whom a distinction between migraine and TTH could not be conclusively made were grouped under unclassifiable headaches. Patients who had secondary headaches, and those with a doubtful epilepsy diagnosis, or who had mental retardation or lesional epilepsy, were excluded.

Patients' demographics, epilepsy duration, frequency of seizures, types of headache, the antiepileptic drugs (AEDs) used, and the temporal relationship between headaches and seizures were recorded. The patients were assessed based on their medical history, observed seizures, and electroencephalography (EEG) findings, and types of seizures were classified as partial, primary generalized, and secondary generalized partial seizures. Headaches were typed on their temporal relationship with seizures as preictal, postictal, or interictal. Headaches beginning within 24 h before a seizure and lasting through seizure onset were classified as preictal headaches, while those beginning within 3 h of seizure onset and lasting for up to 72 h were classified as postictal headaches; headaches without a temporal relationship to a seizure that resolved within 24 h before seizure onset were classified as interictal headaches. The study was approved by the local ethics committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital. The subjects provided signed written informed consent to participate.

## 3. Statistical analysis

The data were transferred to IBM SPSS Statistics software, version 22. The assessment of the study data included descriptive statistics (mean, standard deviation) for numeric variables, and frequency distribution for categorical variables. The relationship between two categorical variables was assessed with the Chi-Squared test, and the difference between more than two independent groups used the one-way analysis of variance (ANOVA).

**Table 1**  
Patients' demographics and clinical characteristics.

Age (years)	30.9 $\pm$ 13.1
Sex	
Female	190 (54.4%)
Male	159 (45.6%)
Epilepsy duration (years)	13.5 $\pm$ 10.9
Seizure frequency	
<1/year (n, %)	132 (37.8%)
$\geq 1$ /year, <1/month (n, %)	42 (12%)
$\geq 1$ /month, <1/week (n, %)	118 (33.8%)
$\geq 1$ /week (n, %)	57 (16.3%)
Seizure type	
Partial seizure (n, %)	69 (19.8%)
Primary generalized seizure (n, %)	209 (57.9%)
Secondary generalized partial seizure (n, %)	71 (20.3%)
Headaches	
Present	152 (43.6%)
Absent	197 (56.4%)
Headache type	
Migraine	94 (26.9%)
TTH	60 (17.2%)
Unclassifiable	43 (12.3%)
Medication (MT/PT)	
Monotherapy	227 (65%)
Polytherapy	122 (35%)

## 4. Results

The study comprised 349 patients (190 females, 159 males). The patients' demographics and clinical characteristics relevant to epilepsy and headaches are shown in Table 1.

Of those patients with epilepsy who experienced headaches, postictal headaches were most frequent (41.6%). Table 2 shows the temporal relationship between headaches and seizures.

A statistically significant relationship could not be established between type of headache (migraine, TTH, or unclassifiable) and the preictal, postictal, or interictal timing of headaches (Table 3).

When considered based on seizure type, preictal headaches were significantly higher ( $p = 0.016$ ) in patients with primary generalized and secondary generalized partial seizures, compared to those with partial seizures; there was no relationship between the types of seizure and postictal or interictal headaches (Table 4).

Headaches were significantly lower in male patients compared to females, and migraine-type headaches were significantly higher in female patients compared to males ( $p = 0.006$ ). Migraine-type headaches were less common in patients who experienced less than one seizure per year, but significantly higher in patients who experienced more than one seizure per month, or less than one per week ( $p = 0.017$ ). A significant relation was not found between type of headache and seizure type. Migraine-type headaches were significantly higher in patients receiving monotherapy compared to those receiving polytherapy ( $p = 0.015$ ) (Table 5).

## 5. Discussion

Headache is a common symptom in patients with epilepsy and the general population, and therefore the prevalence of primary headache in

**Table 2**  
Temporal relationship between headaches and seizures in patients with epilepsy.

	n (%)
Preictal headache	19 (9.6%)
Postictal headache	82 (41.6%)
Interictal headache	17 (8.6%)
Preictal + postictal headache	33 (16.8%)
Preictal + postictal headache	4 (2%)
Postictal + interictal headache	26 (13.2%)
Preictal + postictal + interictal headache	16 (8.1%)

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