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EDITORIAL



Dear Colleagues,

We are pleased to present our second issue of 2026, featuring another selection of interesting articles.

Artificial intelligence is increasingly becoming a part of our lives. The number of articles generated using this method is also growing day by day. Journals screen every article for potential plagiarism, but no consensus has yet been reached regarding articles produced using AI. We are interested in hearing your views and opinions on this matter.

I would also like to mention that a brief presentation on the current status of our journal will be given at the general assembly of the National Epilepsy Congress. We look forward to your participation.

Best wishes.
S. Naz Yeni, M.D., Prof.
Editor-in-Chief

Epilepsy and Respiratory System: A Multidisciplinary Approach to Diagnosis and Treatment - A Literature Review

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Abstract

Epilepsy is a chronic neurological disorder characterized by recurrent seizures, with a multifactorial etiology. This literature review aims to explore multidisciplinary models for the diagnosis and treatment of epilepsy, with particular focus on the relationship between epilepsy and the respiratory system. In November 2024, we systematically searched Google Scholar and PubMed using the following keywords: “epilepsy” or “seizure”, “respiratory system”, “hyperventilation”, “treatment”, “multidisciplinary”, “rehabilitation”, and “physiotherapy”. Epileptic seizures have been shown to affect various physiological systems, including the respiratory system. Specific brain regions involved in seizure activity overlap with areas responsible for respiratory regulation, suggesting a potential bidirectional relationship between seizures and respiratory dysfunction. Respiratory problems induced by seizures may develop into chronic complications and pose serious health risks for individuals with epilepsy. Conversely, pre-existing or seizure-induced respiratory dysfunctions may increase seizure frequency. This review aims to raise awareness of respiratory complications in people with epilepsy and highlights the need for a multidisciplinary approach, including neurology, pulmonology, rehabilitation, and physiotherapy, in the assessment, treatment, and follow-up of these patients. Further research should investigate the effectiveness and structure of multidisciplinary team models in epilepsy care.

Keywords: Epilepsy, respiratory system, physical therapy

INTRODUCTION

Epilepsy is a chronic, non-communicable brain disease that affects approximately 50 million people worldwide.^{1,2} It is characterized by an imbalance between excitatory and inhibitory neural activity, resulting in hyperexcitability and recurrent seizures.³

Seizures are triggered by abnormal, synchronous neuronal firing in brain networks, often due to structural, infectious, or metabolic abnormalities.⁴ Epilepsy affects individuals across all age groups and genders. However, structural-metabolic causes and perinatal trauma are the most frequent etiologies in the 5-9 age group (46%), whereas brain developmental disorders are predominant in children under 4 years (23%). In patients aged 60 and older, cerebrovascular disease accounts for 44% of cases.⁵

Seizures cause a range of physiological responses, with autonomic dysfunction being particularly notable. During a seizure, abrupt activity in central autonomic centers can alter heart rate and respiration. Notably, a decrease in respiratory frequency has been reported, especially in temporal lobe seizures. No significant difference in respiratory rate⁶ was observed between left- and right-sided seizures.

The respiratory centers in the brainstem, such as the medulla oblongata and the pons, are susceptible to seizure-induced electrical disturbances. Seizure activity may provoke respiratory changes, particularly in generalized and mesial temporal lobe seizures. These changes include desaturation, obstructive apnoea, hypoventilation, hypercapnia, acidosis, bradypnoea, and tachypnoea.⁷

Although evidence links epileptic seizures to hyperventilation (HV), few studies have comprehensively assessed the respiratory system in patients with epilepsy. Therefore, this review aims to (1) increase awareness of respiratory alterations in epilepsy and (2) emphasize the importance of a multidisciplinary treatment approach.

Epileptic Seizures and Respiratory Function

Epileptic seizures can directly and indirectly influence respiratory function, and conversely, respiratory impairments can exacerbate seizure susceptibility.

Respiratory Effects During and After Seizures

- Respiratory disorders in the ictal period: epileptic seizures have the potential to cause temporary cessation or disorganization of breathing. Especially tonic-clonic seizures,² which have a tonic phase followed by clonic muscle contractions, have the potential to obstruct the airways during muscle contraction and thus prevent oxygen intake.⁸
- Respiratory disorders in the postictal period include alterations in respiratory rate and depth following a seizure. Some individuals may experience respiratory pauses, medically termed postictal apnoea, for a few minutes following the seizure.⁹

Respiratory Conditions as Seizure Triggers

- Respiratory tract infections may increase seizure risk through systemic inflammation, fever, hypoxemia, and associated metabolic disturbances. The development of symptomatic seizures in patients with respiratory diseases is associated with blood gas changes, including hypoxemia and respiratory acidosis.¹⁰
- Reduced oxygen levels (hypoxemia) can impair cerebral function and result in seizures. The clinical manifestations are analogous to those observed in idiopathic epilepsy. However, epileptic seizures associated with acute hypoxia are frequently accompanied by pathological changes, including neuronal ischaemic necrosis and foci of partial cortical softening.¹¹

HV and Seizure Activity

HV is defined as rapid breathing, whether deep or shallow that can result in a significant and abnormal decrease in carbon dioxide (CO₂) levels or an increase in blood pH. Although the physiological purpose of HV is to increase oxygen levels, it can cause a sensation of breathlessness or dizziness. In severe instances, it can result in syncope and even loss of consciousness.¹²

Two have been described to explain why HV may trigger seizures in patients with epilepsy. The first mechanism involves cerebral vasoconstriction due to hypocapnia, leading to reduced cerebral blood flow rather than true hypoxia. The second is decreased CO₂ levels in the blood, a condition known as hypocapnia.¹³ Indeed, sufficient evidence suggests that such conditions may increase the incidence of epileptic seizures. However, contrary to popular assumptions, the occurrence of HV after exercise is associated with fewer seizures than isolated HV.¹⁴ The underlying reason for this is that the body requires HV as a natural adaptive response to exercise. In summary, the underlying mechanism is different from that of isolated HV.¹⁵

Respiratory Complications in Epilepsy

The relationship between epilepsy and respiratory function is characterized by a reciprocal and intricate interplay. It is reasonable to conclude that the respiratory issues observed in epilepsy may reflect complex underlying mechanisms. Seizures

can directly affect respiration, leading to alterations in respiratory patterns, such as apnoea or oxygen desaturation. In particular, many individuals with epileptic encephalopathy exhibit altered breathing patterns, including periodic and irregular breathing.¹⁶ Central apnoeas, defined as transient cessation of breathing, can occur during seizures or independently, and may contribute to oxygen desaturation and potential respiratory failure.¹⁷ Conversely, respiratory dysfunction, such as chronic hypoventilation, may influence seizure susceptibility and increase the severity of seizures.¹⁸

The development of hypoventilation, frequently accompanied by hypercapnia (elevated CO₂ levels), can result in chronic respiratory compromise and exacerbate breathing difficulties.¹⁹

Sudden Unexpected Death in Epilepsy (SUDEP)

SUDEP has an incidence ranging from 0.09 to 9 per 1,000 patient-years, with the highest incidence observed in patients with intractable epilepsy.²⁰ Both cardiac and respiratory mechanisms play a role in SUDEP.²¹ Seizures are associated with hypoxemia.^{22,23} Previous studies have shown that the incidence of ictal/postictal hypoxemia is high among patients with localization-related epilepsy who underwent inpatient video-electroencephalography telemetry. In partial-onset seizures,²⁴ ictal hypoxemia may be severe and prolonged.

Treatment Approaches in Epilepsy and Their Respiratory Implications

Antiepileptic drugs have historically been the primary treatment for epilepsy, aiming to control seizures and reduce their frequency and severity.¹¹ However, some pharmaceutical agents used in the management of epilepsy may have adverse effects on cardiovascular function and respiration.⁶ Several studies have reported that some antiepileptic drugs exacerbate respiratory depression or increase sleepiness, which can lead to irregular breathing patterns.¹¹ However, the prevalence of drug-resistant epilepsy poses significant challenges for seizure control.²⁵ Therefore, evaluation of different therapeutic options and approaches is needed.

Today, epilepsy surgery is considered a viable approach for cases where antiepileptic drugs are inadequate. This procedure involves the surgical removal of the epileptogenic focus or lesion, with the objective of achieving seizure freedom, particularly in cases where the lesion is well-defined.²⁶ Nevertheless, it is imperative to carefully weigh the potential risks of such a procedure, including the possibility of neurological deficits, against the anticipated benefits. It is evident that non-surgical and non-pharmacological methods that carry a reduced risk of complications. These include vagal nerve stimulation (VNS), transcutaneous VNS, deep brain stimulation, trigeminal nerve stimulation, transcranial direct current stimulation, transcranial magnetic stimulation, as well as emerging and experimental approaches such as gene and stem cell therapies.²⁷ In patients with epilepsy, it is crucial to closely monitor their breathing patterns during any surgical procedure performed under general anesthesia. This is because certain antiepileptic drugs, particularly benzodiazepines, can interact with anesthetic drugs and reduce respiratory function.²⁸

Physiotherapy and Multidisciplinary Management

Sleep and respiratory problems, which are frequently reported in patients with epilepsy, significantly affect patients' daily functioning and quality of life. Therefore, epilepsy treatment should not be limited to medical interventions alone; patients should be managed with a multidisciplinary approach. Respiratory rehabilitation is a therapeutic approach that aims to enhance respiratory muscle strength, augment musculoskeletal system endurance, and augment exercise tolerance. It encompasses breathing exercises, strength and flexibility training, aerobic exercise, airway hygiene practices, and energy conservation techniques.

The most commonly prescribed respiratory rehabilitation exercises are breathing exercises, due to their ease of performance, cost-effectiveness, and suitability for the majority of patients. Instruction in posture exercises, effective coughing techniques, energy-conservation techniques, and respiratory-control techniques will facilitate superior rehabilitation outcomes when combined with respiratory exercises tailored to the patient's specific needs.

It is hypothesized that aerobic exercise may reduce respiratory problems by increasing the vital capacity of the lungs. In a published review, aerobic exercise was recommended as a safe form of exercise for individuals with epilepsy.¹⁴ The majority of studies employed an aerobic exercise intensity based on at least 60% of the maximum heart rate, at least 60% of peak VO_2 max, or a moderate level on the Graded Perceived Exertion Scale. A published report analyzed specific activities to determine which were safe for patients with epilepsy. Athletic activities, including bowling, judo, wrestling, baseball, basketball, football, volleyball, skiing, and dancing, as well as racquet sports, were identified as safe for patients with epilepsy.¹⁴

Yoga represents another potential avenue for intervention in patients with epilepsy who present with respiratory complications and other comorbidities. The practice of yoga, which encompasses a range of mental and physical techniques such as meditation and relaxation, has been demonstrated to enhance lung function by fostering increased awareness of breathing.²⁹

One of the most significant comorbidities associated with epilepsy is sleep apnea. In addition to conventional treatments, other treatment modalities have been reported in the medical literature.

Myofunctional therapy (MT) is a therapeutic modality described in the literature for improving tongue positioning and nasal breathing. There is a substantial body of evidence demonstrating the efficacy of MT in the treatment of sleep apnoea. MT comprises isotonic and isometric exercises for the oral and oropharyngeal structures.³⁰

Another method, orofacial MT (OMT), seeks to enhance muscle tone, endurance, and movement capacity of the pharyngeal and peripharyngeal muscles. Recent studies have demonstrated the efficacy of OMT in reducing the incidence of snoring, apnoea, and daytime sleepiness and improving the quality of nocturnal sleep.³¹

DISCUSSION

In studies evaluating respiratory function in patients with epilepsy, respiratory function test results are lower than expected. Table 1 lists selected studies from the literature.

Despite significant progress in elucidating various aspects of epilepsy, the management of the disease still entails substantial risks and continues to pose numerous clinical challenges. It is well established that epileptic seizures can lead to a wide range of secondary complications, some of which are well recognized, while others remain underexplored. Among these, respiratory complications are particularly critical, including sleep apnea, impaired respiratory control, and associated cognitive and behavioral disturbances.

Given the severity and frequency of respiratory dysfunctions in individuals with epilepsy, it is imperative to raise awareness among clinicians and researchers of the importance of a multidisciplinary approach to the diagnosis and management of epilepsy. In this context, physiotherapy-based interventions should not only be seen as supportive but also as preventive components of treatment, with the potential to complement pharmacological and surgical approaches.

Integrating physiotherapy into epilepsy care may indirectly contribute to seizure management by improving respiratory function, sleep quality, physical conditioning, and overall quality of life, thereby supporting pharmacological and surgical treatment approaches. Therefore, future research and clinical practice should prioritize collaborative care models that include neurologists,

Table 1. Results regarding epilepsy and respiratory evaluations

Study	Sample size	Evaluation and assessment	Main results
Gökçek et al. (2021) ³²	30 individual aged 18-40 years with generalized epilepsy	Demographic data number of seizures per week, dyspnea with modified Medical Research Council, pulmonary function, level of physical activity with international physical assessment survey	Respiratory function and physical activity were affected
Pavlova et al. (2013) ³³	43 adult patients aged 22-62 years with seizure like non-epileptic events (SLNE)	Pulse oxymetry, electrocardiography and respiratory inductance plethysmography	Cardiorespiratory dysfunction, specifically bradypnea apnea, preictal bradycardia and oxygen saturation is more frequently seen in SLNE
Brotherstone et al. (2020) ³⁴	119 participants (65 children and 54 adults) with an age range of 0.66-62.1 years	Heart rate change and oxygen saturation were analysed from electroencephalography videotelemetry	Indicate that the novel algorithm can detect clinically significant seizures
Berilgen et al. (2004) ³⁵	A total of 32 epileptic patients (23 generalized, 9 partial epilepsy) and 32 healthy volunteers	Sympathetic skin response, for evaluating the sympathetic nervous system, respiratory function tests (RFTs)	No abnormalities were observed on RFTs in patients with either partial or generalized epilepsy

physiotherapists, pulmonologists, and other allied health professionals to optimize the overall management of epilepsy.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.G., Concept: Ö.G., B.S., P.K., Design: Ö.G., B.S., P.K., Data Collection or Processing: Ö.G., B.S., P.K., Analysis or Interpretation: Ö.G., Literature Search: Ö.G., M.B., P.K., Writing: Ö.G., M.B., B.S., P.K., G.K.

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Morphometric Measurements of the Corpus Callosum in Juvenile Myoclonic Epilepsy Patients and Their Prognostic Value in Disease Course

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Abstract

Objective: Juvenile myoclonic epilepsy (JME) is an idiopathic generalized epilepsy syndrome with age-dependent onset. The corpus callosum (CC), the largest commissural pathway connecting the two cerebral hemispheres, has been reported to undergo structural alterations in epilepsy. However, data regarding morphometric CC changes in JME patients and their prognostic implications remain limited. This study aimed to determine whether regional differences exist in CC morphometric measurements in JME patients and whether these measurements have prognostic value.

Methods: Magnetic resonance imaging scans of 40 JME patients and 20 age- and sex-matched healthy controls were evaluated. CC measurements were obtained from midsagittal T1-weighted images and included the anterior-posterior (A-P) diameter and the perpendicular diameters of the genu, truncus, and splenium.

Results: A total of 40 patients with JME and 20 healthy controls were included. The genu thickness of the CC was significantly reduced in patients compared with controls, whereas the truncus, splenium, and A-P diameters did not differ. In sex-based analyses, male patients showed a greater A-P diameter than female patients, while no sex differences were observed among controls. No correlations were identified between CC measurements and age, disease duration, seizure type, or seizure frequency. Patients receiving polytherapy and patients treated with valproic acid exhibited significantly larger A-P diameters than patients receiving monotherapy and patients treated with levetiracetam, respectively.

Conclusion: JME is associated with region-specific structural alterations of the CC, particularly a reduced thickness of the genu. These changes appear unrelated to clinical severity markers such as seizure type, frequency, or disease duration, suggesting a predominantly developmental or genetic basis. The enlarged A-P diameter observed in male patients and those receiving valproic acid or polytherapy may reflect sex- or treatment-related influences on callosal morphology. Further prospective studies using advanced imaging modalities are needed to clarify the clinical significance of these findings.

Keywords: Juvenile myoclonic epilepsy, corpus callosum, morphometry, prognosis, magnetic resonance imaging

INTRODUCTION

Juvenile myoclonic epilepsy (JME), a common idiopathic generalized epilepsy syndrome, typically emerges during adolescence and is characterized by irregular, arrhythmic myoclonic jerks that often occur shortly after awakening, and is associated with a genetic predisposition and a generally favorable response to antiseizure medications. Generalized tonic-clonic seizures (GTCS) are frequently reported, while absence seizures occur less commonly. Electroencephalography classically demonstrates generalized spike-and-wave or polyspike-wave discharges, and photosensitivity is frequently observed.¹

The corpus callosum (CC), the largest commissural fiber tract, plays a critical role in interhemispheric integration of motor, sensory, and cognitive functions. Its subregions—genu, truncus, isthmus, and splenium—may exhibit structural variability due to variations in myelination, developmental anomalies, and demographic or clinical factors.²⁻⁶

The CC has been implicated in seizure propagation, with callosotomy studies suggesting involvement in both excitatory and inhibitory interhemispheric mechanisms. Although neuroimaging is not required for the diagnosis of JME in neurologically normal patients, increasing evidence indicates structural and functional abnormalities within the thalamocortical and frontal networks. Advanced imaging modalities have reported alterations in cortical gray matter, frontal lobe organization, CC morphology, and broader white matter connectivity.⁷⁻¹¹

While CC abnormalities have been described in several epilepsy syndromes,¹²⁻¹⁴ morphometric changes specific to JME remain insufficiently characterized. This study aimed to evaluate regional CC morphometry in JME and to explore potential associations with clinical characteristics.

METHODS

This study was approved by the University of Health Sciences Türkiye, Ankara Training and Research Hospital Clinical Research Ethics Committee (approval no: 390/2020, date: 20.08.2020). Forty patients with JME aged ≥ 20 years who were followed at a tertiary epilepsy clinic and 20 age- and sex-matched healthy controls were included. Exclusion criteria were age < 20 years (due to incomplete CC development), use of non-antiepileptic drugs, intellectual disability, comorbid conditions, alcohol or substance use, and refusal to participate. Written informed consent was obtained. JME diagnosis was based on the 1989 the International League Against Epilepsy classification and the 2011 Avignon and the 2012 The Hague consensus criteria.^{1,15} Clinical and demographic data (age, sex, age at onset, disease duration, seizure type and frequency, and antiepileptic drugs) were recorded for patients; only demographic data were collected from controls.

Magnetic resonance imaging (MRI) scans with 3D T1-weighted sequences were used to obtain midsagittal images of the CC. Measurements included anterior-posterior (A-P) perpendicular diameters of the genu, truncus, and splenium. The maximum CC length was measured on midsagittal slices, with perpendicular lines used to obtain regional diameters. All measurements were manually performed by the same researcher.

Statistical Analysis

Data were analyzed using SPSS. Categorical variables were expressed as counts and percentages; continuous variables were expressed as mean \pm standard deviation or median (minimum-maximum). Normality was assessed by visual inspection and the Kolmogorov-Smirnov and Shapiro-Wilk tests. Non-normally distributed data were compared using the Mann-Whitney U or Kruskal-Wallis tests; normally distributed data were compared using the independent t-test or analysis of variance. The chi-squared test was applied to categorical variables. Correlations between numerical variables were examined using Spearman's rank correlation test. A p-value 0.05 was considered significant.

MAIN POINTS

- This study investigated the morphometry of the segments of the corpus callosum (CC).
- These measurements were compared between juvenile myoclonic epilepsy (JME) patients and a healthy population.
- The results showed that the CC anterior-posterior diameter was thinner in females than in males.
- JME patients showed thinning of the CC genu, and no relationship was found between the morphological measurements of the CC segments and disease duration, age at onset, seizure type, or seizure frequency.

RESULTS

The study population was divided into two groups: patients (n=40) and controls (n=20). The patient group ranged in age from 21 to 47 years (mean age, 33.1 years) and consisted of 28 females and 12 males. The control group comprised 13 females and 7 males, with ages ranging from 20 to 50 years (mean age, 34.1 years). There were no statistically significant differences between the groups in age or gender distribution ($p > 0.05$). In the patient group (n=40), the disease duration ranged from 3 to 40 years, with a mean of 18.2 years. The age at first seizure in the patient group ranged from 2 to 30 years, with a mean of 14.7 years. In the patient group (n=40), 23 patients (57.5%) exhibited GTCS combined with myoclonus and absence seizures, while 17 patients (42.5%) had GTCS and myoclonus without absence seizures (Table 1).

Regarding antiseizure medications, 20 patients (50%) were using levetiracetam (LEV), 24 (60%) valproic acid (VPA), and 3 (7.5%) lamotrigine (LTG). Median daily doses were 1000 mg for both LEV and VPA, and 150 mg for LTG (Table 1). Patients were classified according to seizure frequency, as detailed in Table 2.

Among those with myoclonic seizures, 55% were seizure-free during follow-up. Seventy-five percent of patients with GTCS were seizure-free. Among those with absence seizures, 60.9% were seizure-free. Full seizure frequency distributions are shown in Table 2.

The MRI measurements of the CC were compared between the patient and control groups, revealing a statistically significant difference in the genu measurements ($p < 0.05$). These findings are presented in Table 3 and illustrated in Figure 1.

Table 1. Demographic and clinical characteristics of the study groups

	Patient group	Control group	p-value
Age (years)	33.1 \pm 7.6	34.1 \pm 8.7	0.648
Gender (female/male) (n)	28/12	13/7	0.922
Seizure type (n) (myoclonus/GTCS/absence)	40/40/23		
Disease duration (years) [mean (min-max)]	18.2 (3-40)		
Age at first seizure (years) [mean (min-max)]	14.7 (2-30)		
Drug, mg (median dose, min-max)			
LEV (n=20)	1000 (500-2000)		
VPA (n=24)	1000 (250-1500)		
LTG (n=3)	150 (25-200)		

GTCS: Generalized tonic-clonic seizures, LEV: Levetiracetam, VPA: Valproic acid, LTG: Lamotrigine

Table 2. Seizure frequency distribution in the patient group

	GTCS (n=40)	Myoclonus (n=40)	Absence (n=23)
Seizure-free	30 (75%)	22 (55%)	14 (60.9%)
≤ 1 seizure/month	7 (17.5%)	7 (17.5%)	7 (30.4%)
≤ 1 seizure/week	3 (7.5%)	5 (12.5%)	1 (4.3%)
> 2 seizures/week	-	6 (15%)	1 (4.3%)

GTCS: Generalized tonic-clonic seizures

In the control group, no sex-related differences were identified in CC measurements. In the patient group, males had a significantly larger A-P diameter than females ($p=0.037$), while measurements of the genu, truncus, and splenium showed no sex-based differences (Table 4 and Figure 2). No significant correlations were observed between age and CC morphometric parameters in either patients or controls ($p>0.05$).

When patients were classified as receiving monotherapy ($n=33$) or polytherapy ($n=7$), the polytherapy group exhibited a significantly larger A-P diameter ($p=0.005$). No significant group differences were found in measurements of the genu, truncus, or splenium (Table 5).

When CC measurements were analyzed by medication type, the thicknesses of the genu, truncus, and splenium did not differ between LEV ($n=13$) and VPA ($n=17$) users. However, patients receiving VPA had a significantly greater A-P diameter ($p=0.041$; Table 6).

In the patient group, potential correlations between disease duration and segmental CC measurements on MRI were investigated; no statistically significant relationships were found ($p>0.05$). Similarly, no significant correlations were found between age at onset and the segmental CC measurements on MRI ($p>0.05$). Potential associations between seizure types (GTCS/myoclonus/absence) and segmental CC measurements on MRI were also investigated, revealing no statistically significant relationships ($p>0.05$).

Table 3. Mean±SD of the MRI measurements and p-values based on the patient and control groups

	Thickness, mm, mean±SD	p-value
Patient's genu	10.6±1.4	0.002
Control's genu	11.9±1.6	
Patient's truncus	5.7±1.8	0.74
Control's truncus	5.8±0.8	
Patient's splenium	9.9±1.5	0.09
Control's splenium	10.6±1.2	
Patient's A-P	66.6±5.1	0.84
Control's A-P	66.5±4.5	

SD: Standard deviation, MRI: Magnetic resonance imaging, A-P: Anterior-posterior

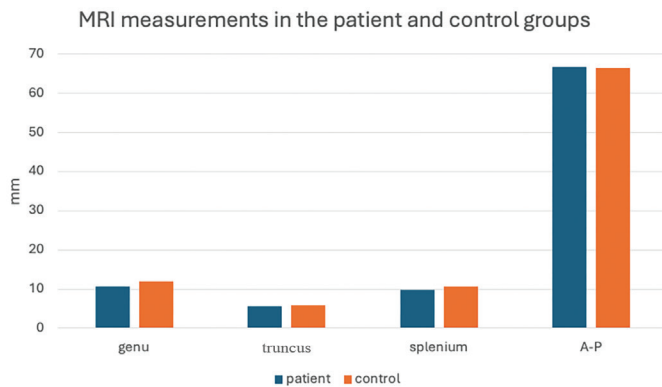


Figure 1. Comparison of MRI measurements between the patient and control groups
MRI: Magnetic resonance imaging, A-P: Anterior-posterior

DISCUSSION

The CC, the largest commissural pathway, demonstrates morphological variability influenced by factors such as myelination, axonal loss, developmental anomalies, genetics, and demographic characteristics, including age and sex.¹⁶⁻¹⁸ Structural CC alterations, particularly in regions responsible for interhemispheric motor network integration, have been previously documented in JME.¹⁹ However, studies specifically assessing sex-related differences in CC morphology within JME cohorts are lacking, as most previous investigations have focused on comparisons between JME patients and healthy controls.^{11,19} Given that sex-related

Table 4. Corpus callosum measurements by sex (patient group)

Patient	Female (n=28)	Male (n=12)	p-value
MRI-genu	22.21	16.50	0.156
MRI-truncus	20.09	21.46	0.734
MRI-splenium	18.91	24.21	0.189
MRI-A-P	17.98	26.38	0.037

MRI: Magnetic resonance imaging, A-P: Anterior-posterior

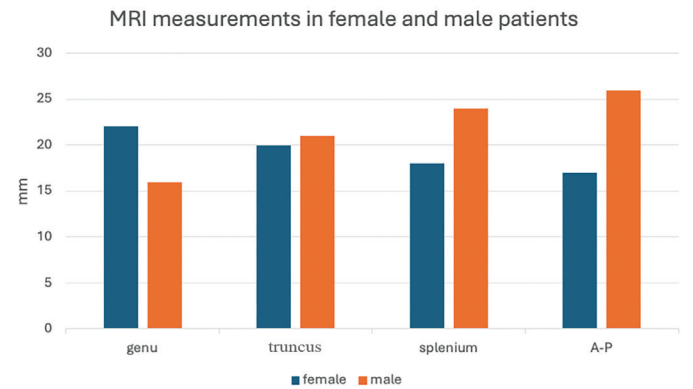


Figure 2. Comparison of MRI measurements between male and female patients in the patient group
MRI: Magnetic resonance imaging, A-P: Anterior-posterior

Table 5. Corpus callosum measurements in monotherapy vs polytherapy

	Polytherapy (n=7)	Monotherapy (n=33)	p-value
MRI-genu	20.86	20.42	0.929
MRI-truncus	14.64	21.74	0.144
MRI-splenium	25.50	19.44	0.213
MRI-A-P	31.64	18.14	0.005

MRI: Magnetic resonance imaging, A-P: Anterior-posterior

Table 6. Corpus callosum measurements in patients using LEV vs VPA

	LEV (n=13)	VPA (n=17)	p-value
MRI-genu	13.96	16.68	0.455
MRI-truncus	15.38	15.59	0.942
MRI-splenium	14.54	16.24	0.598
MRI-A-P	11.81	18.32	0.041

LEV: Levetiracetam, VPA: Valproic acid, MRI: Magnetic resonance imaging, A-P: Anterior-posterior

variations in CC thickness and white matter microstructure are well established in healthy populations,^{20,21} the evaluation of sex-specific CC morphology within JME constitutes an important but underexplored area. In our study, male patients exhibited a significantly greater anteroposterior (A-P) diameter than female patients; no such difference was observed among controls. This suggests that, beyond biological sex, disease-related factors may contribute to callosal variation in JME.

The CC has been implicated in seizure generalization, and corpus callosotomy has been shown to reduce seizure frequency in refractory epilepsy.^{7,22} Conversely, the occurrence of seizures following CC sectioning, or in cases of CC agenesis, suggests a possible inhibitory role for the CC.²²⁻²⁴ Neuroimaging studies have also demonstrated CC abnormalities in epilepsy, including reduced size and altered white matter integrity.²³⁻²⁵ Further evidence indicates that the genu may be a key pathway for seizure propagation.²⁴

Recent findings linking CC atrophy with neuronal dysfunction support this notion. Sandoval Karamian et al.²⁵ reported a reduced size of the genu in newborns with genetic epilepsies, suggesting that white matter abnormalities may be a common feature in genetically mediated epilepsies. The smaller genu measurements observed in our JME cohort are consistent with a potential genetic contribution.

The relationship between CC structure and cognitive function has also been explored. Atkinson et al.²⁶ reported that CC areas were smaller in epilepsy patients and correlated with IQ but not with memory or language dominance. JME, characterized by genetic predisposition and age-specific onset, has been associated with structural abnormalities in thalamocortical and frontal networks.²⁷ Diffusion MRI studies revealed altered microstructural connectivity in the anterior CC and widespread loss of white matter integrity in JME, potentially explaining frontal cognitive dysfunction.^{28,29} Anastasopoulou et al.¹¹ further suggested that callosal abnormalities may distinguish JME from other generalized epilepsies.

While monotherapy remains the standard initial approach to epilepsy management, polytherapy is required for adequate seizure control in more complex cases. Increased antiepileptic drug burden has been reported to influence large-scale neural network organization and white matter microstructure.^{26,27} Therefore, assessing CC morphology across treatment subgroups may illuminate both disease-related structural changes and treatment-response dynamics. To date, no human studies have directly compared CC morphometry between patients treated with VPA and those treated with LEV. However, experimental evidence indicates that VPA exposure can affect myelination and brain volumetry,²¹ and CC morphology has been associated with treatment response in epilepsy.²⁰ The larger A-P diameter observed in VPA-treated and polytherapy patients in our cohort may thus reflect treatment-related effects, longer disease duration, greater seizure burden, or complex interactions among these factors. Evaluating CC morphology in JME with respect to sex and antiseizure medication type addresses a notable gap in the current literature.

Importantly, our study demonstrated a significantly reduced genu thickness in JME patients compared with controls; however, these differences were not associated with disease duration, seizure

type, or seizure frequency. This supports the hypothesis that CC alterations in JME are predominantly neurodevelopmental or genetic rather than secondary to chronic epilepsy.^{29,30} Prior research on this topic has produced mixed findings. Volumetric studies generally report no association between CC size and clinical features,²⁹ consistent with our results. In contrast, diffusion-based studies have identified subtle anterior callosal abnormalities associated with longer disease duration, suggesting that progressive microstructural changes may occur in a subset of patients.^{28,29} These divergent findings likely arise from methodological differences, including variations in imaging modalities (macrostructural vs. microstructural), patient characteristics, and analytic approaches. Overall, the evidence suggests that CC alterations in JME are primarily determined by genetic or developmental factors, although secondary microstructural changes related to disease progression cannot be entirely ruled out.

The absence of correlations between CC morphology and clinical variables in our cohort raises important questions about the temporal evolution of white matter abnormalities in JME, specifically whether they precede seizure onset or emerge over the course of the disease. Future research integrating advanced neuroimaging, larger cohorts, genetic analysis, and neuropsychological assessment is necessary to clarify these mechanisms. Such studies may improve prognostic stratification, inform individualized treatment planning, and support earlier identification of at-risk individuals.

Study Limitations

Participants with comorbid conditions were excluded from the study due to the potential confounding effects on the measurements. Additionally, incorporating genetic and psychological evaluations could further enhance the robustness of our findings.

CONCLUSION

This study demonstrated region-specific alterations in the CC in patients with JME, characterized by reduced genu measurements and increased CC A-P diameter in specific subgroups. These findings suggest that CC involvement in JME may reflect a multifactorial process influenced by biological factors, such as sex, as well as treatment-related characteristics, including antiepileptic drug exposure and polytherapy. The absence of associations between CC morphology and clinical variables, including disease duration and seizure features, supports the possibility that callosal alterations may be related to underlying neurodevelopmental or genetic mechanisms rather than acquired effects of epilepsy. Given the retrospective design and limited subgroup sample sizes, these results should be interpreted cautiously. Prospective studies incorporating advanced imaging methods, larger cohorts, and genetic and cognitive assessments are warranted to clarify the clinical significance of CC changes and determine whether CC morphology may serve as a structural marker in JME.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Ankara Training and Research Hospital Clinical Research Ethics Committee (approval no: 390/2020, date: 20.08.2020).

Informed Consent: Written informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ü.E., Concept: Ü.E., S.K.G., Design: Ü.E., S.K.G., Data Collection or Processing: Ü.E., Analysis or Interpretation: Ü.E., Literature Search: Ü.E., Writing: Ü.E., S.K.G.

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

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Association of Brain-derived Neurotrophic Factor (rs6265) Gene Polymorphism with Susceptibility to Epilepsy

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Abstract

Objective: This study aimed to measure serum brain-derived neurotrophic factor (BDNF) and neuronal nitric oxide synthase (nNOS) levels in Egyptian children with epilepsy, to calculate the frequencies of *BDNF* gene polymorphisms to elucidate their usefulness as biomarkers for diagnosing epilepsy and assessing drug response.

Methods: Serum BDNF and nNOS levels were measured by enzyme-linked immunosorbent assay in 60 epileptic children as well as in 30 healthy children of the same age and sex. The BDNF rs6265 polymorphism was evaluated by genomic TaqMan genotyping.

Results: The genotyping distribution of the *BDNF* gene did not differ significantly between the controls and epileptic cases. The homozygous (G/G) responded to treatment far better. Mean serum BDNF was substantially less than the controls. However, children with epilepsy had considerably higher mean serum nNOS concentration.

Conclusion: BDNF genotypes have a big impact on responsiveness to therapy. In epileptic children, the mechanism of epileptogenesis is influenced by serum BDNF and nNOS.

Keywords: Brain-derived neurotrophic factor, neuronal nitric oxide synthase, gene polymorphism, epilepsy

INTRODUCTION

Epilepsy is a neurological condition that affects 0.5-1% of people globally, it results in aberrant neuronal discharge.^{1,2} Fisher et al.³ described the independent occurrence of two or more unprovoked seizures is known as epilepsy. They are not classified as febrile or neonatal seizures, either separately or in combination and are typified by involuntary motor, sensory, or autonomic seizures. Various pieces of evidence have suggested that epilepsy may be caused by genetic variations, even if the exact cause of the condition is still unknown. Over 70% of people with epilepsy are thought to have hereditary susceptibility.⁴ The effectiveness of treatment can be impacted by genetic anomalies that change electrical impulses, channel function, neuronal excitability, and possibly even the pharmacokinetics of antiepileptic drugs (AEDs).⁵

The most abundant neurotrophic factor in the brain is a tiny dimeric protein called brain-derived neurotrophic factor (BDNF). While it has a modest affinity for the p75 receptor, it has a high binding affinity for the tyrosine kinase receptor B. Several intracellular cascades, such as the signaling route for mitogen-activated protein kinase are activated because of these attachments promote both development and survival in a range of neurons. Research has demonstrated that it weakens inhibitory gamma-aminobutyric acid synapses while strengthening excitatory (glutamatergic) ones. BDNF enhances neurogenesis and contributes to activity-dependent synaptic plasticity such as learning and memory.⁶

The 5' proregion of the human BDNF protein is altered by a single-nucleotide polymorphism (SNP) that replaces methionine (met) at codon 66 (Val66met) with valine (Val), which is irrelevant to position 196 of exon 2 (rs6265). This polymorphism affects activation dependent BDNF synthesis at the synapse, axonal transport, and intracellular packing of pro-BDNF.^{7,8}

There is evidence linking neuronal nitric oxide synthase (nNOS) to epileptogenesis. Both kainic acid-induced seizure rat models and a status epilepticus mouse model generated by electrical stimulation exhibited increased nNOS levels.^{9,10} According to Akyuz et al.,¹¹ nNOS

inhibition may have an anticonvulsant impact since it raises the epileptic threshold when nNOS activity is blocked.

This study aimed to assess the association of the *BDNF* (rs6265) gene polymorphism with epilepsy susceptibility in Egyptian patients, and to evaluate serum BDNF and nNOS levels as biomarkers of disease severity and treatment response in childhood epilepsy.

METHODS

Patients

A total of 90 Egyptian youngsters (58 boys and 32 girls) were enrolled in this comparative case-control study. The study included 60 children with epilepsy and 30 apparently healthy, demographically and ethnically matched controls. Between December 2021 and October 2022, patients with epilepsy were selected from our institution's pediatric neurology outpatient clinic.

Based on the children's medical history and an electroencephalogram (EEG), the diagnosis of epilepsy was reached. Following a third seizure within two months, all study participants were placed on antiepileptic medication, and they underwent clinical, biochemical, and EEG evaluations every three months.

The cases studied were chosen randomly from children who had experienced seizures over the previous 12 months. The parents provided a written informed consent prior to the children's enrolment in the study. Every patient underwent a thorough clinical examination and medical history taking.

Exclusion Criteria

The following were the exclusion criteria:

- Patients who are older than 15 years old.
- Patients who have epilepsy because of diseases including meningitis or encephalitis, head trauma, brain tumors, or inadequate oxygen exposure during birth.
- Patients with developmental abnormalities including autism and neurofibromatosis.
- Patients with an unpredictable seizure frequency.
- Patients with inadequate medical records.

MAIN POINTS

- The combined evaluation of genetic and biochemical markers may contribute to improved understanding of epilepsy pathophysiology and potential biomarker development.
- Children with epilepsy exhibited significantly lower serum brain-derived neurotrophic factor (BDNF) levels and significantly higher neuronal nitric oxide synthase (nNOS) levels compared with healthy controls.
- No significant difference was observed in the distribution of the BDNF rs6265 (Val66Met) polymorphism between patients and controls; however, patients with the homozygous G/G genotype showed a significantly better response to antiepileptic therapy than heterozygous G/A patients.
- Serum BDNF and nNOS levels were identified as significant predictors of treatment response and resistance, supporting their potential role as biomarkers in pediatric epilepsy.

Blood Samples

Early in the morning, during the interictal phase, blood samples were taken. Five milliliters of blood were collected from patients by venipuncture. Samples were divided into two parts. The first part was added to ethylenediamine-tetra acetic acid (EDTA) tube, and the other part was added to plane tube. The EDTA tubes were preserved at -80 °C until the extraction of genomic DNA. The plane tubes were centrifuged, and sera were obtained and frozen at -20 °C.

I. BDNF Genotyping

1) The Extraction of DNA

QIA amp DNA mini kit (QIAGEN, Lot No. 169017038) was used to extract the DNA. DNA was extracted according to manufacturer's instructions.

2) SNP Genotyping

SNP genotyping was done using TaqMan SNP genotyping assays.

Assay ID: C_11592758_10.

Catalog number: 4351379.

SNP ID: rs6265.

Product Description

TaqMan SNP genotyping assays provide optimized assays for genotyping SNPs. The products use the 5' nuclease assay for amplifying and detecting specific SNP alleles in purified genomic DNA samples. Each assay allows researchers to genotype individuals for a specific SNP.

SNP Genotyping Assay Contents

The 40XSNP genotyping assay contains:

- Sequence-specific forward and reverse primers to amplify the polymorphic sequence of interest.
- Two TaqMan® minor groove binder probes:
 - One probe labeled with VIC® dye detects the allele 1 sequence.
 - One probe labeled with FAM™ dye detects the allele 2 sequence.

Context Sequence (VIC/FAM):

TCCTCATCCAACAGCTCTTCTATCA (G/A) GTGTTTCGAAAGTGTC AGCCAATGAT

II. Measuring BDNF Serum Level

SinoGeneClon Biotech enzyme-linked immunosorbent assay (ELISA) kit for quantitative determination of human BDNF concentrations (Cat: SG-00371) was utilized to measure the serum level of BDNF using the ELISA. According to the manufacturer's instructions, the intra-assay coefficient of variation was <8%, and the inter-assay coefficient of variation was <10%.

III. Measuring nNOS Serum Level

To measure the blood level of nNOS, we used the ELK Biotechnology ELISA kit for quantitative detection of human nNOS concentrations (Cat: ELK1619). According to the manufacturer's instructions, the intra-assay coefficient of variation was <8%, and the inter-assay coefficient of variation was <10%.

nNOS assay specificity and limitations: the ELISA kit used was specific for nNOS with no reported cross-reactivity with endothelial NOS or inducible NOS isoforms. Limitations of the method include its indirect nature and inability to assess enzymatic activity.

Samples were analyzed as single measurements due to limited sample volume and in accordance with the manufacturer's recommendations. Assay reliability was ensured by standardized procedures and acceptable intra- and inter-assay coefficients of variation.

Statistical Analysis

The collected data was coded and checked before entering data into a computer. The statistical package for the social sciences version 23 software was used to statistically analyze the data, which was then shown in tables and graphs. Following a Kolmogorov-Smirnov test for normality, the quantitative data were displayed as mean and standard deviation for a normal distribution and median and IQ for a non-normal one. Frequencies and percentages of the qualitative data were displayed, and the p-value was obtained by comparing them using chi-square. A p-value of less than 0.05 denoted statistical significance in every analysis.

Clinical Definitions

Treatment response was categorized based on previously published criteria: seizure freedom was defined as excellent response, $\geq 75\%$ reduction in seizure frequency as very good response, these thresholds are consistent with established definitions of clinically meaningful seizure reduction reported in prior studies (World Health Organization, practical neurology, neurology reviews).

1. Excellent Response for Treatment Response in Epilepsy

Definition: complete seizure freedom during the follow-up period (i.e., 0% seizure frequency compared to baseline).

2. Very Good Response

Definition: $\geq 75\%$ reduction in seizure frequency compared to baseline.

In some cases, patients had to change medication due to incomplete control of seizures, or they had to add a 2nd medication.

Ethics Clearance and Participation Consent

The study complied with the Declaration of Helsinki's ethical guidelines; the study protocol was approved by Sohag University Faculty of Medicine Medical Research Ethics Committee (approval no: IRB00013006, date: 11/10/2021) and was registered on ClinicalTrials.gov (ID: NCT05096871). The parents provided

written informed consent prior to the children's enrolment in the study.

RESULTS

This study involved the enrollment of 60 epileptic patients (61.7% males and 38.3% females) and 30 controls. The mean age of the patients was 7.8 ± 3.6 years, with a range of 2 to 15 years. Seventy percent of children with epilepsy had generalized tonic-clonic seizures, while 18.3% had focal seizures. The remaining children had syncopal attacks (5%) and absence seizures (6.7%). The illness lasted an average of 3.6 ± 2.5 years, with a range of 1 to 10.5 years. All patients in this study were on AED as shown in Table 1.

Serum BDNF and nNOS concentrations in control group and epileptic children. The study patients' group had a significantly lower mean BDNF concentration (6.7 ± 0.87 ng/mL) compared to the controls (9.49 ± 1.43 ng/mL) ($p < 0.001$). Additionally, the epileptic children's mean serum nNOS concentration was significantly higher (5.8 ± 2.9 ng/mL) compared to the controls ($1.6 \pm 2.91.24$ ng/mL) ($p < 0.001$) as shown in Table 2.

There was no significant difference in the genotyping distribution of the BDNF gene between the epileptic cases and the controls ($p = 0.643$), as shown in Table 3.

The genotyping frequencies in both the cases and controls are not significantly different from what would be expected if the population is in the Hardy-Weinberg equilibrium. The Hardy-Weinberg equation of cases (p-allele freq. = 0.80/q-allele freq. = 0.12) and controls (p-allele freq. = 0.83/q-allele freq. = 0.17).

Based on *BDNF* gene polymorphism when comparing patients with heterozygous G/A and homozygous G/G, there were no significant differences in age, height, weight, or duration of epilepsy ($p = 0.435$, 0.265, 0.352, and 0.457 respectively) as shown in Table 4.

Table 1. Participant demographic information and attributes

Variables	Mean±SD	Range
Age (years)	7.8±3.6	2-15
Duration of the disease (years)	3.6±2.5	1 to 10.5
	n	Percent
Gender (cases)		
Male	37	61.7%
Female	23	38.3%
Types of seizures		
GTCC	42	70%
Focal	11	18.3%
Syncopal attack	3	5%
Absence seizures	4	6.7%
Response to treatment		
Excellent	9	15%
Very good	12	20%
On regular treatment	1	1.7%
Add second medication	26	43.3%
Change medication	12	20%

The data are displayed as a number (%), median (range), and mean±SD. GTCC: Generalized tonic clonic seizures, SD: Standard deviation

Table 2. Comparison of serum BDNF and serum neuronal NOS concentrations (ng/mL) between the cases and controls

Parameter	Epileptic cases n=60	Control group n=30	p-value by Mann-Whitney U test
Serum BDNF (ng/mL) (mean±SD)	6.7±0.87	9.49±1.43	<0.001***
Median (IQR)	6.7 (6.0:7.4)	9.0 (8.6:10.6)	
Range	5:8.1	7.4:12.2	
Serum nNOS (ng/mL) (mean±SD)	5.8±2.9	1.6±1.24	<0.001***
Median (IQR)	5.7 (3.6:8.17)	1.0 (0.7:2.2)	
Range	0.7:12.3	0.5:5.7	

***: p<0.001 for extremely significant, and NS for non-significant p>0.05. For extremely significant, use NOS.

nNOS: Neuronal nitric oxide synthase, BDNF: Brain-derived neurotrophic factor, SD: Standard deviation, IQR: Interquartile range, NS: Non-significant

Table 3. Genotyping distribution of *BDNF* gene in epileptic cases and control group in the study

Genotyping	Groups	Total		p-value by chi-square	
		Epileptic cases n=60	Control group n=30		
Heterozygous G/A	No (% within groups)	23 (38.3%)	10 (33.3%)	33 (36.7%)	*0.643 (NS)
Homozygous G/G	No (% within groups)	37 (61.7%)	20 (66.7%)	57 (63.3%)	
Total	Count	60	30	90	

*: Non-significant p>0.05 denotes non-significant.

NS: Not significant, BDNF: Brain-derived neurotrophic factor

Table 4. Comparison of age, weight, height, duration of epilepsy among cases (n=60) according to BDNF genotype

Parameter	<i>BDNF</i> gene polymorphism		p-value by Independent t-test
	Homozygous G/G n=37	Heterozygous G/A n=23	
Age (years)	8.13±3.8	7.3±3.5	0.435 (NS)
Weight (kg)	28.59±10.6	25.4±10.4	0.265 (NS)
Height (cm)	126.59±19.2	121.9±17.5	0.352 (NS)
Duration of epilepsy (years)	3.85±2.7	3.36±2.1	0.475 (NS)

Non-significant p>0.05 is indicated by NS.

BDNF: Brain-derived neurotrophic factor, NS: Not significant

Table 5 shows that there was no significant difference between the homozygous and heterozygous epileptic cases in terms of family history (p=0.958), seizure type (p=0.411), or EEG characteristics (p=0.416), on the other hand on assessing the patients' response to therapy, it shows that the homozygous group had significantly better response to medication (p=0.032).

The results also revealed that age, height, weight, and duration of sickness did not substantially correlate with serum BDNF or serum nNOS, while as shown in Table 6 there were positive moderate correlations with response to medication in the serum BDNF dependent and nNOS dependent groups. No correlations were found between other parameters.

Table 7 demonstrates that there was excellent overall negative correlation between BDNF and nNOS levels and slightly moderate negative correlation among cases. However, there were non-significant negative correlations among control groups.

According to the linear regression analysis, the results demonstrated that height, weight, age and disease duration were non-significant risk factors associated with serum BDNF concentrations. While serum BDNF and serum nNOS were significant predictors of treatment response (p=0.000 and 0.010, respectively) as shown in Table 8.

Table 9 demonstrates that resistance to antiepileptic therapy was significantly predicted by the serum BDNF levels (p=0.000) with cut-off point <6.87 ng/mL, area under curve (AUC) =0.946, sensitivity 81.6%, specificity 95.2% and accuracy rate 94.6%. Serum nNOS was also a significant predictor of resistance to antiepileptic treatment with p=0.000, (cut-off point >5.05, AUC=0.819, sensitivity 87.9%, specificity 81.0% and accuracy rate 81.9%).

Figure 1 shows the allelic discrimination plot for SNP rs6265 where the scatter plot displays the results of genotyping using a TaqMan SNP assay. Each point represents an individual sample plotted according to normalized fluorescence intensities for the G and A alleles. Two distinct clusters are observed: samples homozygous for the G allele (red, G/G) and heterozygous samples (green, G/A). No clear cluster corresponding to homozygous A/A (blue) was detected, and no samples fell into the undetermined category. This distribution suggests that in the analyzed population, the G allele is prevalent, with individuals observed as either homozygous G/G or heterozygous G/A, while the A/A genotype was absent in this dataset.

DISCUSSION

The complex neurological disorder known as epilepsy is characterized by frequent, unexpected seizures and temporary

Table 5. Cross tabulation of family history, type of seizure, EEG features and response to medication in 60 cases according to genotyping

Family history		Genotyping		Total	X ²	p-value
		Homozygous G/G	Heterozygous G/A			
No	Count (%)	32 (86.5%)	20 (87%)	52 (86.7%)	0.003	0.958
Yes	Count (%)	5 (13.5%)	3 (13%)	8 (13.3%)		
Total	Count	37	23	60		
Type of seizures		Homozygous G/G	Heterozygous G/A	Total	X ²	p-value
GTCC	Count (%)	26 (70.3%)	16 (69.6%)	42 (70%)	2.87	0.411 (NS)
Focal	Count (%)	8 (21.6%)	3 (13%)	11 (18.3%)		
Syncopal attacks	Count (%)	2 (5.4%)	1 (4.3%)	3 (5%)		
Absence seizures	Count (%)	1 (2.7%)	3 (13)	4 (6.7%)		
Total	Count	37	23	60		
EEG features		Homozygous G/G	Heterozygous G/A	Total	X ²	p-value
Generalized activity	Count (%)	27 (73%)	16 (69.6%)	43 (71.7%)	1.75	0.416 (NS)
Focal activity	Count (%)	6 (16.2%)	2 (8.7%)	8 (13.3%)		
Normal	Count (%)	4 (10.8%)	5 (21.7%)	9 (15%)		
Total	Count	37	23	60		
Response to medication		Homozygous G/G	Heterozygous G/A	Total	X ²	p-value
Excellent	Count (%)	8 (21.6%)	1 (4.3%)	9 (15%)	10.57	0.032*
Very good	Count (%)	10 (27%)	2 (8.7%)	12 (20%)		
On regular treatment	Count (%)	1 (2.7%)	0 (0%)	1 (1.7%)		
Add second medication	Count (%)	14 (37.8%)	12 (52.2%)	26 (43.3%)		
Change medication	Count (%)	4 (10.8%)	8 (34.8%)	12 (20%)		
Total	Count	37	23	60		

*p<0.05 (significant), NS: A non-significance level of p>0.05.

GTCC: Generalized tonic clonic seizures, EEG: Electroencephalography

Table 6. Eta correlation of family history, sex, EEG features and response to treatment with serum BDNF and serum neuronal nitric oxide synthase 60 cases

Correlation coefficient	Serum-BDNF (dependent)	Serum neuronal nitric oxide synthase (dependent)
Sex (n=90)	eta=0.014 p=0.91 (NS)	eta=0.48 (NS) p=0.48 (NS)
Type of seizures (n=60)	eta=0.303 p=0.315 (NS)	eta=0.2 (NS) p=0.90 (NS)
EEG features (n=60)	eta=0.278 p=0.143 (NS)	eta=0.106 (NS) p=0.5 (NS)
Family history (n=60)	eta=0.001 p=0.9 (NS)	eta=0.06 (NS) p=0.608 (NS)
Response to tilt table test (n=60)	eta=0.754 p=0.000***	eta=0.547 (NS) p=0.000***

NS: A non-significance level of p>0.05, ***, p<0.001 (very highly significant), weakly correlated (0.2-0.4); moderately correlated (0.4-0.6); and excellently correlated (0.6-1).

NS: Not significant, EEG: Electroencephalography, BDNF: Brain-derived neurotrophic factor

disruptions in brain activity. It is mostly brought on by pathologic neuronal discharges.¹²

BDNF has been identified over the past decade as one of the key neurotrophic factors that may regulate neuronal morphology and synapse formation, contributing to the central nervous system's neuroprotective function. Studies using transgenic mouse models have also shown that increased neuronal excitability and epilepsy risk may be influenced by brain overexpression of BDNF.¹³ Since SNPs are among the most significant genetic alterations that could control BDNF expression and metabolism, recent studies have

increasingly focused on these variants. Several studies have shown that the most prevalent polymorphism in the *BDNF* gene, rs6265 G>A, results in an amino acid change from Val to met, which may contribute to various central nervous system disorders including Alzheimer's disease, Parkinson's disease, depression, and bipolar disorder.^{7,14-17}

Although the role of neuronal nitric oxide in epilepsy is well established, its anticonvulsant or proconvulsant effects remain controversial. While numerous studies have investigated the relationship between proinflammatory cytokines or nNOS and

Table 7. Spearman's rho correlation of serum BDNF and serum neuronal NOS

Correlation between BDNF and nNOS	Correlation coefficient	p-value
Overall (n=90)	-0.714**	0.000
Cases (n=60)	-0.444**	0.000
Controls (n=30)	-0.207 (NS)	0.2

**At the 0.01 level (2-tailed), the correlation is significant, NS is not.

NS: Not significant, NOS: Nitric oxide synthase, BDNF: Brain-derived neurotrophic factor

Table 8. Linear regression analysis of important study parameters as predictors of response to treatment

Parameters	Unstandardized coefficients		Standardized coefficients	t	Significant
	B	Std. error	Beta		
1 (Constant)	3.573	0.803		4.451	0.000
Age	0.024	0.035	0.179	0.672	0.504 (NS)
Weight	-0.011	0.009	-0.250	-1.254	0.215 (NS)
Height	0.003	0.007	0.119	0.420	0.676 (NS)
Disease duration	-0.001	0.023	-0.007	-0.056	0.956 (NS)
Serum BDNF	-0.361	0.055	-0.653	-6.599	0.000***
Serum NOS	0.044	0.016	0.265	2.665	0.010**

Dependent variable: response to medication. Strong significance by **p<0.01 and very high significance by ***p<0.001. Significantly not (NS: p>0.05).

NOS: Nitric oxide synthase, BDNF: Brain-derived neurotrophic factor, Std: Standard

Table 9. Sensitivity, specificity and accuracy rate of serum neuronal nitric oxide synthase and serum BDNF conc. as predictors of resistance to epileptic treatment in studied patients

Variable	Cut-off point	Area under the curve	p-value	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy rate
Serum BDNF (ng/mL)	<6.87	0.946	0.000***	81.6%	95.2%	96.9%	75%	94.6%
Serum nNOS (ng/mL)	>5.05	0.819	0.000***	87.9%	81.0%	88.2%	69.2%	81.9%

***p<0.001 (very highly significant).

nNOS: Neuronal nitric oxide synthase

epilepsy, the potential role of these factors in pediatric absence epilepsy remains unclear.¹⁸ Accordingly, the present study was conducted to evaluate the association between epilepsy susceptibility and the *BDNF* rs6265 gene polymorphism.

In the current study, epileptic patients had a mean disease duration of 3.6±2.5 years, with a range of 0.5-10.5 years. Among the epileptic cases, 23 patients were female (38.3%) and 37 were male (61.7%). The control group comprised 21 males (70.0%) and 9 females (30.0%). Statistical analysis revealed no significant difference in sex distribution between the case and control groups (p=0.436). These findings are consistent with previous studies reporting a slightly higher risk of epilepsy in males. For example, Karabiber et al.¹⁹ reported a male-to-female ratio of 1.42:1 in Turkish children aged 1-12 years, Wong²⁰ reported a ratio of 1.22:1, and Aaberg et al.²¹ observed a marginally higher incidence of epilepsy in males. However, other studies, such as that by Topbaş et al.,²² have reported an equal or slightly higher prevalence among females.

The results of the present study demonstrated that blood BDNF levels were significantly lower in epileptic patients compared with the control group (p<0.001). In contrast, serum nNOS levels were significantly higher in epileptic patients than in controls (p<0.001).

These findings are consistent with the study by Poniatowski et al.,²³ which reported significantly lower serum BDNF levels in patients with generalized tonic-clonic seizures compared with controls. However, these results partially contradict the meta-analysis by Nowroozi et al.,¹⁴ which found no significant differences in BDNF levels between patients with epilepsy and control subjects, except for lower BDNF levels observed in individuals with partial epilepsy.

Numerous studies investigating nNOS have reported inconsistent findings. Ibragic et al.²⁴ found no statistically significant difference in nNOS levels between patients with epilepsy and control subjects. In contrast, Kovács et al.,²⁵ Ribeiro et al.,²⁶ and Arhan et al.,²⁷ reported higher nNOS levels in newly diagnosed patients with epilepsy. These discrepancies may be attributed to the heterogeneity of epilepsy, as well as differences in study populations, sample sizes, and methodological approaches.

In the present study, the genotypic distribution of the *BDNF* gene was evaluated in both patients with epilepsy and controls. The heterozygous G/A genotype was observed in 38.3% of epileptic cases, while the homozygous G/G genotype was present in 61.7%. Among controls, 33.3% were heterozygous for G/A and 66.7% were homozygous for G/G. No statistically significant difference

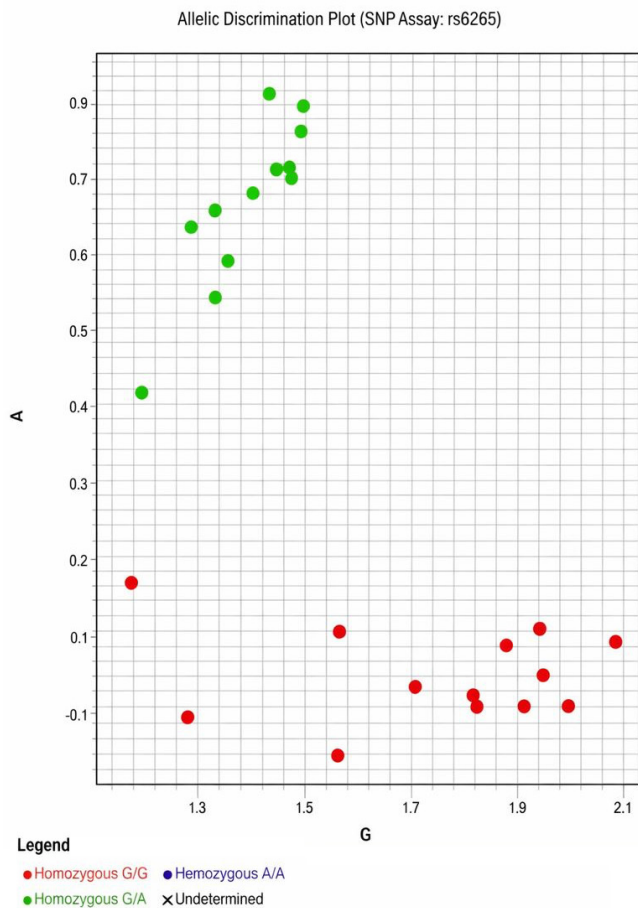


Figure 1. The allelic discrimination plot for SNP rs6265
SNP: Single-nucleotide polymorphism

was observed in the distribution of BDNF genotypes between epileptic patients and controls ($p=0.643$).

The BDNF Val66Met polymorphism affects activity-dependent secretion and intracellular trafficking of BDNF and has been implicated in epilepsy. Several studies have reported an association between the BDNF Val66Met polymorphism and epilepsy susceptibility.

Previous studies suggest that the impact of BDNF polymorphisms on epilepsy may vary across populations. Xu et al.¹⁷ and Sha'ari et al.²⁸ reported that Asian populations may be more susceptible to epilepsy due to BDNF polymorphisms. Similar associations have been observed in patients with fragile X syndrome²⁹ and in Japanese cohorts.³⁰ Nevertheless, conflicting findings have also been reported, as Lohoff et al.³¹ failed to replicate the Japanese data, and Bragatti et al.³² found no significant clinical effect of the polymorphism in temporal lobe epilepsy.

In the present study, patients carrying the homozygous genotype showed a significantly better response to antiepileptic medication than heterozygous carriers ($p=0.032$), with no significant differences between groups in age, height, weight, or disease duration.

Consistent with these findings, Zeev et al.³³ reported that individuals homozygous for the wild-type BDNF allele (Val/Val)

had milder disease severity than heterozygous carriers (Val/Met). In Rett syndrome patients with the p.R168X mutation, the presence of the BDNF polymorphism was associated with increased disease severity and a higher seizure risk. Together, these data suggest that the BDNF Val66Met polymorphism may influence both disease severity and treatment response in epilepsy.^{7,8,34}

Study Limitations

Notwithstanding the noteworthy discoveries and contributions of the present investigation, it is important to recognize certain limitations:

1. Sample size: The study's findings may not be as broadly applicable as they could be due to its comparatively small sample size. More solid results and increased conclusion reliability would come from a larger sample size.

2. Selection bias: Because study participants were chosen from a certain demographic or medical environment, selection bias may have been introduced. This might limit the results' ability to be applied to a larger population and compromise the sample's representativeness.

3. Measurement variability: The measurement of serum BDNF and nNOS may have inherent variability due to assay methods or laboratory procedures. Variations in sample handling, storage, and analysis could introduce measurement errors that might affect the accuracy and reliability of the results. Moreover, a potential limitation of this study is the reliance on ELISA-based measurement of nNOS, which reflects circulating protein levels rather than direct enzymatic activity or tissue expression.

4. Generalizability: The findings of this study might be specific to the studied population or setting and may not be directly applicable to other populations or geographic regions. Further studies with diverse populations are needed to validate the results across different contexts.

5. Confounding factors: Case-control studies may be prone to confounding variables, where the observed association between the exposure (serum BDNF and nNOS levels) and outcome (response to treatment) may be influenced by other variables that were not accounted for in the study design or analysis.

6. Temporality: Case-control studies are retrospective in nature, meaning that the exposure and outcome are assessed simultaneously or after the occurrence of the outcome. This makes it challenging to establish a clear temporal relationship between exposure and outcome, limiting the ability to determine causality.

It is important to consider these limitations when interpreting the findings of a case-control study and to recognize the need for further research, such as prospective cohort studies, to confirm the observed associations and address these limitations.

CONCLUSION

This study demonstrates that pediatric epilepsy is associated with decreased serum BDNF levels and increased nNOS levels, supporting the involvement of neurotrophic and nitric oxide-related pathways in epilepsy pathophysiology. While no significant difference was observed in the overall distribution of the BDNF rs6265 (Val66Met) polymorphism between patients and controls,

the polymorphism was associated with clinical response to treatment. Homozygous carriers showed a significantly better response to antiepileptic therapy than heterozygous carriers, suggesting a potential influence of BDNF genetic variation on disease severity and therapeutic outcome. These findings underscore the relevance of BDNF as a potential biomarker and therapeutic modifier in pediatric epilepsy, warranting further large-scale studies to validate these results.

Ethics

Ethics Committee Approval: The study protocol was approved by Sohag University Faculty of Medicine Medical Research Ethics Committee (approval no: IRB00013006, date: 11/10/2021).

Informed Consent: The parents provided written informed consent prior to the children's enrolment in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.S., Concept: A.M.F., S.K.A-M., N.S.A., A.A.S., R.S.Y., Design: A.M.F., S.K.A-M., N.S.A., A.A.S., R.S.Y., Data Collection or Processing: A.M.F., S.K.A-M., A.A.S., Analysis or Interpretation: A.M.F., S.K.A-M., N.S.A., A.A.S., R.S.Y., Literature Search: A.M.F., S.K.A-M. A.A.S., R.S.Y., Writing: N.S.A., R.S.Y.

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

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Seizure Control in Patients with Dual Pathologies

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Abstract

Objective: Temporal lobe epilepsy (TLE) is the most common focal epilepsy syndrome and remains medically refractory in a substantial proportion of patients. Dual pathology, defined as the coexistence of hippocampal sclerosis with an additional neocortical lesion, is an important cause of surgical failure when not adequately recognized. This study aimed to evaluate the clinical characteristics and postoperative seizure outcomes of patients with dual pathology compared with those with isolated mesial temporal sclerosis.

Methods: We retrospectively reviewed 125 patients who underwent surgery for TLE between January 2005 and February 2023. Thirty-one patients with dual pathology, defined as hippocampal sclerosis accompanied by a neocortical tumor, were included. A control group consisted of 34 age-matched patients with isolated mesial temporal sclerosis. Clinical features, seizure characteristics, surgical procedures, postoperative outcomes assessed using the Engel classification, and complications were analyzed.

Results: The mean age was similar between the dual pathology and control groups. However, the age at seizure onset was significantly later in patients with dual pathology (26.5±15.9 years vs. 9.2±7.8 years; p<0.001). Generalized tonic-clonic seizures were more frequent in the dual-pathology group, whereas focal seizures with impaired awareness predominated in patients with isolated mesial temporal sclerosis. Engel class I seizure freedom was achieved in 61.3% of patients with dual pathology and in 67.6% of controls, with no significant difference between groups. Postoperative complication rates were comparable.

Conclusion: Despite differences in seizure characteristics and age at seizure onset, postoperative seizure outcomes in patients with dual pathology were comparable to those in patients with isolated mesial temporal sclerosis when both the mesial temporal structures and the associated neocortical lesion were adequately resected. Dual pathology should be considered in patients with TLE who present with mesial temporal sclerosis accompanied by a neocortical tumor, particularly in those with a relatively late age at seizure onset.

Keywords: Dual pathology, epilepsy, resective surgery

INTRODUCTION

Epilepsy is one of the most prevalent neurological disorders globally, affecting approximately 65 million people.¹ Despite advancements in pharmacological treatments, nearly one-third of patients continue to experience medically refractory seizures. Among these individuals, mesial temporal lobe epilepsy (TLE) stands out as a frequent and particularly intractable form, with hippocampal sclerosis (HS) being its most commonly identified pathological correlate. Histopathologically defined by selective neuronal loss and gliosis in the hippocampus, HS is well recognized as a key epileptogenic substrate and a frequent target of resective epilepsy surgery.²

However, in a notable proportion of patients—estimated at 5-20%—HS is not the sole pathological finding.^{3,4} Instead, it coexists with other distinct structural abnormalities, most commonly focal cortical dysplasia, low-grade tumors, or vascular malformations.^{2,5} This phenomenon, termed dual pathology (DP), refers to the coexistence of HS with an extrahippocampal lesion, either visible through neuroimaging or revealed via histopathological evaluation.⁶ While the relationship between these lesions remains unclear—whether one initiates or exacerbates the other, or both arise from shared developmental or acquired processes—their co-existence complicates the localization of the epileptogenic zone and the planning of surgical intervention.⁷

The recognition and proper management of DP are critical for optimizing surgical outcomes. In many cases, seizure freedom is only achieved when both the sclerotic hippocampus and the associated lesion are resected. Conversely, failure to detect a secondary lesion, particularly if occult on imaging, may result in incomplete surgery and persistent postoperative seizures. Moreover, the presence of DP has been associated with a greater seizure burden and more complex neurocognitive profiles.

Despite its clinical importance, DP remains underrecognized and understudied. The variability in presentation, the potential subtlety of extrahippocampal lesions, and the limitations of routine imaging all contribute to diagnostic and therapeutic challenges.

In this context, the present study aims to investigate the prevalence, characteristics, and clinical implications of DP in patients undergoing surgery for drug-resistant TLE, with particular attention to histopathological findings and postoperative outcomes.

METHODS

We conducted a retrospective study of 125 patients who underwent surgery for TLE at the Department of Neurosurgery, Bursa Uludağ University, between January 2005 and February 2023. Among these, 31 patients had DP (HS accompanied by neocortical tumors), and 34 age-matched control patients had mesial temporal sclerosis (MTS) and underwent amygdalohippocampectomy.

All patients underwent a standardized preoperative evaluation that included detailed assessment of seizure semiology, prolonged scalp video-electroencephalography (video-EEG) monitoring, and magnetic resonance imaging (MRI). MRI examinations were performed using an epilepsy-dedicated protocol on a 1.5-Tesla system (Siemens Magnetom Aera). The imaging protocol included thin-slice three-dimensional T1-weighted sequences to evaluate cortical thickness and gray-white matter junction abnormalities, as well as high-resolution axial and coronal T2-weighted and FLAIR sequences aligned with the hippocampal axis.^{8,9} In patients with DP, early postoperative contrast-enhanced MRI (24-48 hours postoperatively) was obtained to assess the extent of resection.

Invasive monitoring techniques, such as stereoelectroencephalography or subdural electrode placement, were not required across the cohort. Video-EEG monitoring and continuous video recordings were obtained using scalp electrodes placed in accordance with the International 10-20 electrode mounting system; 16-32-channel reference, longitudinal, and transverse bipolar montages were used. Spikes, sharp waves, spike-and-wave complexes, temporal intermittent rhythmic delta activity, and continuous focal slow-wave activity (theta or delta) were identified. Electrodes with rhythmic theta or delta waves, spike waves, or sharp waves before ictal activity were considered to indicate the localization of the initial ictal activity. Surgical targets

were determined based on concordance among seizure semiology, scalp EEG findings, neuroimaging results, and discussions of the multidisciplinary epilepsy surgery board.

Comprehensive data collection included demographic characteristics, preoperative seizure features, surgical procedures performed, postoperative seizure outcomes, assessed using the Engel classification system, and documented complications. Seizure types were classified according to the International League Against Epilepsy (ILAE) classification.¹⁰ Surgical outcomes were categorized as Engel class I (seizure free or auras only), class ii (rare seizures), class iii ($\geq 75\%$ seizure reduction), or class IV ($< 75\%$ seizure reduction).¹¹

Surgical Technique

Standard surgical treatment for TLE consists of an anterior temporal lobectomy combined with amygdalo-hippocampectomy. This procedure involves resection of variable portions of the anterior and lateral temporal neocortex, followed by intraventricular subpial microsurgical removal of the mesial temporal structures, including the hippocampus and amygdala. The extent of neocortical and mesial resection was determined based on hemispheric dominance, seizure semiology, and anatomical considerations.

In patients with DP, surgical treatment generally consisted of resection of both the mesial temporal structures, as described above, and of the associated neocortical lesion. Depending on tumor location and anatomical constraints, this was achieved by anterior temporal lobectomy combined with lesionectomy or by tailored resections aimed at the complete removal of all radiologically and histopathologically identified epileptogenic substrates. Resection was defined as gross total when no residual tumor was identified intraoperatively or on postoperative MRI, and as subtotal when the residual tumor volume exceeded 5%.¹²

All surgical decisions were made following evaluation by a multidisciplinary epilepsy surgery board, which convenes monthly and comprises neurosurgeons, neurologists specializing in epilepsy, and neuroradiologists. Surgical candidacy was determined based on concordance among seizure semiology, video-EEG findings, neuroimaging results, and clinical characteristics.

Written informed consent for surgical treatment and use of clinical data for research purposes was obtained from all patients prior to surgery. In patients with DP, additional written informed consent was obtained for surgical intervention encompassing both tumor resection and temporal lobectomy. The study was approved by the Medicana Bursa Hospital Clinical Research Ethics Committee (decision no: 2025/08-2, date: 07.10.2025).

Statistical Analysis

We used IBM SPSS 22 for statistical analysis. Continuous variables were expressed as mean \pm standard deviation and analyzed using Student's t-test, while categorical variables were examined using chi-square tests. A p-value < 0.05 was considered statistically significant throughout our analyses.

MAIN POINTS

- Dual pathology (DP) refers to the coexistence of hippocampal sclerosis (HS) with a neocortical tumor or other structural lesion, which complicates epileptogenic zone localization and surgical planning.
- Among 125 patients with temporal lobe epilepsy, 31 had DP (HS+neocortical tumor) and 34 had isolated mesial temporal sclerosis (MTS).
- Seizure onset occurred earlier in MTS patients, while DP patients had later onset and more frequent generalized tonic-clonic seizures.
- Postoperative seizure control rates were comparable (Engel class I: 61.3% in DP vs. 67.6% in MTS), but tumor recurrence occurred in 32.2% of DP patients.
- Resection of both lesions is essential in DP to achieve optimal seizure control with low complication rates.

RESULTS

Demographic and Clinical Characteristics

The study groups showed comparable age distributions (DP: 29.3±14.8 years; MTS: 30±11.2 years, p>0.05). However, gender distribution differed significantly between groups, with a male predominance in the MTS group (70.5%; n=24) compared to the DP group (45.1%; n=14, p=0.047), which was considered in the interpretation of the results.

Age at seizure onset differed significantly: patients with MTS experienced earlier seizure onset (9.2±7.8 years) compared with DP patients (26.5±15.9 years, p<0.001). Seizure semiology also varied substantially between groups. According to the ILAE classification, generalized tonic-clonic seizures predominated in DP cases (54.8%), whereas focal impaired awareness seizures were more characteristic of the MTS group (52.9%). Other seizure types (tonic-clonic, absence, myoclonic) occurred infrequently in both populations (Table 1).

Pathological Findings

Both groups showed a right-sided predominance of lesions [DP: 61.2% (n=19); MTS: 58.8% (n=20)], though this lateralization difference did not reach statistical significance (p>0.05).

In the DP cohort, oligodendroglioma was the most common coexisting pathology in patients with MTS (48.4%, n=15). Among these, 12 cases were classified as World Health Organization (WHO) grade II, while 3 were identified as WHO grade III (anaplastic) (Table 2). Other notable findings included dysembryoplastic neuroepithelial tumors (DNET) (25.8%, n=8), malignant glial tumors (WHO grade III-IV) (12.9%, n=4), and rare tumor types (collectively 12.9%), each represented by a single case: craniopharyngioma, astroblastoma, mixed oligoastrocytoma, and pleomorphic xanthoastrocytoma.

Total resection was achieved in 77.4% of DP cases versus 100% of MTS cases. Follow-up duration averaged 74±35 months for DP patients and 127±28 months for MTS controls.

Postoperative Outcomes

The seizure control outcomes, assessed using the Engel classification system, demonstrated comparable results between the two study groups. In the DP group, 61.3% (n=19) of patients

achieved Engel class I (seizure-free) status, while 67.6% (n=23) of MTS patients achieved the same outcome. The percentages of patients experiencing rare seizures (Engel class II) were similar in both groups: 6.4% (n=2) in DP vs. 5.8% (n=2) in MTS. Notably, 16% (n=5) of DP patients showed no significant improvement (Engel class IV), compared with 11% (n=4) of MTS patients. The mean follow-up duration was significantly longer in the MTS group than in the DP group (127±28 months vs. 74±35 months; Table 3, Figure 1).

Complications

The postoperative complication profiles differed between the two patient groups. In the DP cohort, 6.5% (n=2) of patients required emergency reoperation for intracerebral hematoma, while 9.7% (n=3) developed surgical site infections requiring treatment. The MTS group showed a different complication pattern, with 2.9% (n=1) of patients developing postoperative hydrocephalus. Statistical analysis revealed no significant difference in overall complication rates between the groups (p=0.095) (Table 4).

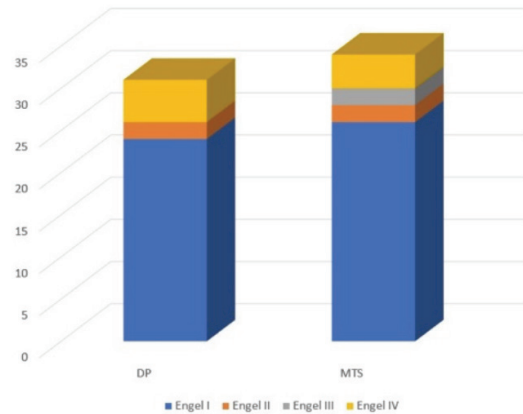


Figure 1. Postoperative outcomes (Engel classification) MTS: Mesial temporal sclerosis; DP: Dual pathology

Table 2. Pathological spectrum in DP

Pathology	n (%)
Oligodendroglioma (WHO grade II-III)	15 (48.4)
DNET	8 (25.8)
Malignant glial tumors (WHO grade III-IV)	4 (12.9)
Craniopharyngioma	1 (3.2)
Astroblastoma	1 (3.2)
Mixed oligoastrocytoma	1 (3.2)
Pleomorphic xanthoastrocytoma	1 (3.2)

DP: Dual pathology, DNET: Dysembryoplastic neuroepithelial tumors, WHO: World Health Organization

Table 3. Postoperative outcomes (Engel classification)

Outcome	DP (%)	MTS (%)	p-value
Class I	61.3	67.6	0.6143
Class II	6.4	5.8	
Class III	0	2.9	
Class IV	16	11	

DP: Dual pathology, MTS: Mesial temporal sclerosis

Table 1. Demographic and clinical characteristics

Variable	DP (n=31)	MTS (n=34)	p-value
Age (years)	29.3±14.8	30±11.2	>0.05
Gender (%)	14 (45.1)	24 (70.5)	0.047*
Seizure onset age (years)	26.5±15.9	9.2±7.8	<0.001*
Seizure types			
- GTC (%)	17 (54.8)	12 (35.2)	
- FIAS (%)	11 (35.4)	18 (52.9)	0.012
- Others (%)	4 (12.9)	4 (11.7)	
Lesion laterality			
- Right	19 (61.2)	20 (58.8)	>0.05
- Left	12 (38.7)	14 (41.1)	

DP: Dual pathology, MTS: Mesial temporal sclerosis, FIAS: Focal impaired awareness seizures, GTC: Generalized tonic-clonic, *: Statistically significant

Table 4. Complication rates

Complication	DP (%)	MTS (%)
Intracerebral hematoma	6.5	0
Surgical site infection	9.7	0
Hydrocephalus	0	2.9

DP: Dual pathology, MTS: Mesial temporal sclerosis

Recurrence

During a mean oncological follow-up of 44.8±35.1 months, tumor recurrence occurred in 32.2% (10 cases) of DP patients. Recurrent cases included 4 oligodendrogliomas (3 WHO grade II and 1 WHO grade III), 2 DNETs, 2 malignant glial tumors (1 WHO grade III and 1 WHO grade IV), and 2 cases of other rare tumor types. The mean time to recurrence was not specifically reported in the study data.

DISCUSSION

Our study demonstrates that, although seizure control rates were slightly lower in the DP group compared with the MTS group, the overall postoperative outcomes were comparable between the groups, and the groups differed in their seizure characteristics.

Most epidemiological features of DP remain controversial due to variations in its definition.¹³ Variations in the definition of DP, low diagnostic sensitivity of MRI, and differences in study populations and methodologies may account for the discrepancies in the reported prevalence of DP and the frequency of associated secondary pathologies.^{14,15} In our study population, 24.2% of patients with drug-resistant epilepsy and HS had DP.

Previous studies have reported a prevalence of DP among patients with TLE that ranges widely, generally from 5% to 20%, depending on diagnostic criteria, imaging sensitivity, and histopathological confirmation.^{3,4,13-15} The relatively higher prevalence observed in our cohort may be partly explained by the inclusion of histopathologically confirmed neocortical tumors and by the long study period, during which improvements in imaging interpretation and surgical pathology likely enhanced recognition of coexisting lesions. Earlier studies have consistently shown that HS is associated with childhood-onset epilepsy, often in the context of febrile seizures, whereas epilepsy related to extrahippocampal structural lesions may present later in life.^{16,17} Consistent with these observations, patients with DP in our series exhibited a significantly later age at seizure onset than those with isolated MTS, suggesting distinct epileptogenic mechanisms and disease trajectories. In instances of DP, excision of both the primary lesion and the HS is essential for improved seizure control.⁴ Occult DP has been reported as one of the causes of failure to achieve seizure control after selective amygdalohippocampotomy in patients with TLE.¹⁸ Occult DP may explain why postoperative seizure outcomes after standard anterior temporal resection for TLE are better than after selective amygdalohippocampotomy, because a more extensive resection increases the likelihood that a neocortical lesion is present in the resected tissue.⁷ Occult DP should always be considered in patients who fail to achieve postoperative seizure control.

Focal cortical dysplasia represents the most common co-occurring pathology in patients with HS.² Our findings revealed a relatively

low prevalence of cortical dysplasia among DP cases. This may be explained by the well-known limitations of MRI in detecting subtle cortical abnormalities. Specifically, cortical dysplasia often remains undetectable on conventional imaging or may resemble gliosis, particularly when accompanied by neuronal and glial proliferation.^{19,20} Consequently, patients with cortical dysplasia in our cohort may have been underdiagnosed, misdiagnosed, or not diagnosed at all. This diagnostic limitation could have led to an underestimation of the true prevalence of DP in our study population.

One significant finding in our cohort was that seizures began much earlier in patients with MTS than in patients with DP. This result is in line with earlier findings that MTS usually manifests early in life, frequently in conjunction with febrile seizures.^{16,17} DP, on the other hand, is more frequently associated with later-onset epilepsy. Since adult-onset seizures are more likely to result in neuroimaging that reveals underlying structural abnormalities, the DP group's older age at seizure onset may affect both diagnostic and treatment timelines.

Furthermore, the observed variations in seizure semiology among the groups could be attributable to differences in epileptogenic networks. Focal impaired awareness seizures were more prevalent in patients with MTS, whereas generalized tonic-clonic seizures were more common in the DP group. This pattern implies that, while MTS usually involves limbic structures and results in more stereotyped seizure manifestations, neocortical lesions in DP cases may promote more rapid seizure generalization or disrupt broader cortical-subcortical circuits.

Although the two groups differed in both underlying pathology and clinical presentation, postoperative seizure freedom rates were comparable, with Engel class I outcomes observed in 61.3% of patients with DP and 67.6% of those with isolated MTS. These results support the effectiveness of surgical intervention in appropriately selected cases. However, a greater proportion of patients in the DP group were classified as Engel class IV (16% vs. 11%), which may reflect the inherent complexity of these cases particularly in achieving complete resection when high-grade or infiltrative tumors are involved, or when the epileptogenic zone is more diffuse. Furthermore, the higher rate observed in the MTS group may be attributable to overlooked focal cortical dysplasia or other occult pathologies.²¹ It is possible that the difference would have been even greater had these pathologies not been missed in the MTS group.

Notably, complete tumor resection was not achieved in approximately 23% of the DP group, which may have further contributed to the group's slightly lower seizure-control rates and the relatively high tumor-recurrence rate of 32.2% observed during follow-up. This is consistent with previous studies reporting a strong association between incomplete resection—especially in low-grade gliomas—and both tumor progression and persistent seizures.²¹ Furthermore, the shorter follow-up period in the DP group (74 months compared to 127 months in the MTS group) may have led to an underestimation of long-term seizure outcomes and recurrence rates.

The DP group demonstrated a heterogeneous histopathological profile, with oligodendroglioma emerging as the most prevalent tumor type, followed by DNET and malignant glial neoplasms. This distribution aligns with previous studies reporting a higher

incidence of certain tumor types—particularly DNET and low-grade gliomas²¹—among patients with pharmacoresistant epilepsy, in whom these lesions frequently coexist with HS in chronic cases. The simultaneous presence of both lesions raises an important and ongoing debate in epilepsy surgery: whether each lesion contributes independently to epileptogenesis or whether one represents the primary epileptogenic focus. In such complex cases—especially when lesions are subtle, multifocal, or radiographically ambiguous—the importance of detailed preoperative planning becomes paramount. High-resolution MRI and complementary imaging modalities, alongside intraoperative tools such as electrocorticography or stereoelectroencephalography, when available, play a crucial role in identifying and guiding the resection of all potentially epileptogenic areas, thereby optimizing surgical outcomes.

Although the overall complication rates were not significantly different between the two groups, the types of complications varied meaningfully. In the DP cohort, a higher incidence of intracerebral hematomas and postoperative infections may be attributed to longer operative durations, more extensive resections, or the technical challenges of removing tumors located near eloquent cortical areas. These differences highlight the importance of tailoring perioperative management strategies according to the specific pathological and anatomical features of each patient.

Study Limitations

Several limitations of this study should be acknowledged. First, the retrospective design and unequal follow-up durations between study groups constitute significant methodological limitations, because the shorter follow-up in the DP group may have led to underestimation of long-term seizure outcomes and tumor recurrence rates. In addition, although age matching was performed, gender matching was not feasible because of the retrospective design and the limited number of patients with DP, resulting in an imbalance in the gender distribution that may be a confounding factor when interpreting the results. Furthermore, the absence of volumetric analysis of tumor burden and the lack of detailed localization of the seizure onset zone using advanced electrophysiological techniques, such as stereoelectroencephalography, limit the precise assessment of the relative epileptogenic contributions of the tumor and the hippocampus in DP cases. Future studies with larger cohorts, a prospective design, and comprehensive electrophysiological mapping are warranted to refine surgical strategies and improve prognostication in this challenging patient population. In addition, multivariate analysis was not performed in this study. Although several factors such as gender, tumor histology, extent of resection, and the presence of infiltrative tumors may influence postoperative seizure outcomes, the relatively small sample size—particularly within the DP subgroup—and the heterogeneity of tumor types limited the ability to construct a reliable multivariate model. Performing such an analysis under these conditions would carry a substantial risk of overfitting and of producing statistically unstable results. Therefore, the findings of this study should be interpreted as exploratory rather than predictive.

CONCLUSION

DP represents an important and potentially underrecognized entity in patients with TLE. Our findings demonstrate that, despite differences in seizure characteristics and age at seizure onset, postoperative seizure control rates in patients with DP are

comparable to those observed in patients with isolated MTS when both the mesial temporal structures and the associated neocortical lesion are adequately resected.

Notably, although age at surgery was similar between the two groups, patients with DP had a significantly later age at seizure onset than those with isolated MTS, who more commonly presented with childhood-onset epilepsy. These findings underscore the importance of considering DP in patients with TLE presenting with MTS accompanied by an additional neocortical lesion and support comprehensive surgical strategies aimed at the resection of all epileptogenic substrates.

Ethics

Ethics Committee Approval: The study was approved by the Medicana Bursa Hospital Clinical Research Ethics Committee (decision no: 2025/08-2, date: 07.10.2025).

Informed Consent: Written informed consent for surgical treatment and use of clinical data for research purposes was obtained from all patients prior to surgery.

Footnotes

Author Contributions: Surgical and Medical Practices: Y.T., P.E., A.B., Concept: P.E., Design: P.E., Data Collection or Processing: Y.T., N.B., Analysis or Interpretation: A.B.D., I.B., A.B., Literature Search: Y.T., P.E., A.B.D., Writing: Y.T., P.E., E.D.

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Identification of Problems Faced by Individuals with Epilepsy in Health Communication

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Abstract

Objective: Individuals with epilepsy often face challenges with medication adherence and health monitoring because communication difficulties that hinder self-expression and information exchange, thereby complicating effective disease management. This study aimed to examine the health communication problems experienced by individuals with epilepsy.

Methods: This descriptive, cross-sectional study was conducted among 172 individuals with epilepsy who presented to the neurology outpatient clinic in eastern and northern Türkiye between August 2023 and August 2024. Study data were collected using the descriptive data form and the health communication problems scale. The independent groups t-test, one-way ANOVA, and Tukey test were used to evaluate the data.

Results: On the health communication problems scale, individuals with epilepsy had mean scores of 2.41±0.53 for the effective communication problems sub-dimension, 2.88±0.80 for the social communication problems sub-dimension, and 2.68±0.72 for the communication barriers sub-dimension. No significant differences were detected in the mean scores for health communication problems among individuals with epilepsy by sex, health expenditure, seizure type, or seizure characteristics ($p>0.05$).

Conclusion: The study revealed that individuals with epilepsy experienced moderate difficulty with health communication. Those who were married, had higher educational attainment, were unemployed, had lower income levels, and were receiving polytherapy experienced greater communication challenges with healthcare professionals.

Keywords: Epilepsy, healthcare professionals, communication barriers

INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures caused by abnormal and excessive electrical discharges in cortical neurons.^{1,2} Epileptic seizures are sudden clinical events marked by spontaneous recurrence and excessive neuronal electrical activity, often accompanied by loss of consciousness.²⁻⁵ Communication is a fundamental process for individuals and society, facilitating relationships and interactions by conveying thoughts, feelings, and information. In this context, health communication is critically important, as individuals' ability to understand medical information, express their needs, and manage their health effectively depends on the quality of communication.⁶⁻¹⁰ Health communication is the exchange of information between individuals or groups regarding health-related issues.¹¹ With advances in healthcare, the importance and application of health communication are increasing across various levels and intensities.^{12,13} Health communication integrates the fields of medical science and communication science.¹⁴ Although it is central to clinical procedures such as diagnosis, treatment, and patient-provider interactions, health communication also encompasses how individuals perceive, interpret, and respond to health-related issues.^{12,14,15} It plays a vital role in developing strategies to manage health problems, understanding symptoms, recognizing risks, and making informed decisions.^{7,16} Moreover, effective health communication contributes to disease prevention, health promotion, and efficient management of medical conditions, producing positive individual, social, institutional, and economic outcomes.¹⁷⁻²⁰ It influences patients' choice of healthcare institutions, their trust in the healthcare system, adherence to treatment, length of hospital stay, and overall quality of care and satisfaction with care.⁷

Epilepsy is a chronic neurological condition that significantly affects the well-being of individuals, families, and societies.²¹ Individuals with epilepsy often experience comorbidities and must carefully manage both their primary condition and associated disorders.^{22,23}

Chronic diseases have profound medical, economic, psychological, and social impacts on individuals, often leading to communication challenges.²⁴ Developing effective self-management strategies for epilepsy requires strong patient-provider communication within a patient-centered approach to care to ensure treatment adherence and to optimize health outcomes.^{22,25}

In managing epilepsy, communication plays an increasingly crucial role. Communication difficulties encountered by individuals during healthcare interactions can hinder self-expression, limit access to adequate information, and compromise disease management. Although previous studies have explored health communication in various populations, no research has specifically addressed the communication problems experienced by individuals with epilepsy. This study aimed to evaluate health communication problems among individuals with epilepsy residing in the northern and eastern regions of Türkiye and to identify factors influencing these problems.

Study Questions

- What are the health communication problems of individuals with epilepsy?
- What are the factors affecting the health communication problems of individuals with epilepsy?

METHODS

This cross-sectional study was conducted in Giresun and Erzurum, located in Northern and Eastern Türkiye, respectively.

Participants

Individuals diagnosed with epilepsy who were followed for at least 6 months at the Neurology Outpatient Clinics of Atatürk University and Giresun University were included in the study. A total of 172 individuals with epilepsy who met the inclusion criteria (being 18 years of age or older, not having cognitive or communication problems, being able to answer the questions in the interview form, and being volunteers for the research) were reached between August 2023 and August 2024 without any sample selection.

Data Collection

The descriptive data form and the health communication problems scale (HCPS) were used to collect the study data.

MAIN POINTS

- Effective health communication is crucial for individuals with epilepsy, as it supports optimal disease management and enhances adherence to treatment. This study explores the communication difficulties encountered by individuals with epilepsy during interactions with healthcare professionals. The findings reveal persistent challenges in understanding medical information, expressing symptoms clearly, and feeling adequately understood by healthcare providers.
- These results underscore the importance of targeted communication training and patient-centered approaches for professionals involved in the care of individuals with epilepsy.
- Enhancing health communication practices may lead to improved clinical outcomes and a higher quality of life for this population.

Descriptive Data Form

The researchers prepared the form, which consisted of 13 questions about age, marital status, sex, education, income, employment status, place of residence, diagnosis period, medication use and number of medications used by individuals with epilepsy, number of seizures in the last year, and seizure types. Loss of consciousness was not evaluated in this study.

Health Communication Problems Scale

The HCPS was developed by Yeşildal et al.²⁶ to identify communication problems experienced by patients in interactions with healthcare personnel. The 5-point Likert-type scale consists of 13 items and three sub-dimensions: effective communication (items 1-6), social communication (items 7-9), and communication barriers (items 10-13). The minimum score that can be obtained on the scale is 13, and the maximum score is 65. Items 1, 2, 4, 5, and 7 of the scale are reverse-coded. As the score on the scale increases, health communication becomes increasingly problematic. The responses on the scale range from 1 (strongly agree) to 5 (strongly disagree). The Cronbach's alpha for the original scale was 0.77,²⁶ and the overall Cronbach's alpha was 0.756 in this study.

Statistical Analysis

The independent groups t-test was used to analyze data from two groups and the one-way ANOVA test was used for three or more groups. Multiple comparisons were made for the results that were significant in the one-way ANOVA, and the Tukey test was used because the data showed homogeneous variances.

Ethical Issues

Written approval was obtained from the Atatürk University Clinical Research Ethics Committee (approval no: 41, date: 26.01.2023). Permission was obtained from the Atatürk University Faculty of Medicine and the Giresun University Department of Neurology. Verbal and written informed consent was obtained from individuals with epilepsy prior to data collection.

RESULTS

Health Communication Problems and Related Factors

Individuals with epilepsy scored 2.41 ± 0.53 on the effective communication problem sub-dimension of the HCPS, 2.88 ± 0.80 on the social communication problems sub-dimension, 2.68 ± 0.72 on the communication barriers sub-dimension, and 2.59 ± 0.51 overall on the HCPS. The effective communication and communication barriers sub-dimensions scored below the obtainable average ($\bar{x}=3.00$), whereas the social communication problem sub-dimension scored close to the obtainable average ($\bar{x}=3.00$) (Table 1).

The mean age of individuals with epilepsy was 37.16 ± 14.83 years, and the mean duration of epilepsy was 14.20 ± 10.64 years. Of the participants, 56.4% were female, 61.6% were married, 45.9% were secondary school graduates, 49.4% lived in the city center, 66.9% were unemployed, 57.6% had income lower than expenses, 33.7% experienced one seizure per year, 50.6% had an undetermined seizure type, and 50% were on polytherapy (Table 2).

Table 1. The distribution of epilepsy patients' scores on the sub-dimensions of the health communication problems scale (n=172)

		Scale and sub-dimensions			
		Effective communication problem	Social communication problem	Communication barriers	Total
Possible scores on the scale	Min-max	1-5	1-5	1-5	1-5
Score received by individuals with epilepsy	Min-max	1.00-3.83	1.00-4.33	1.00-4.50	1.15-3.85
	$\bar{X} \pm SD$	2.41 \pm 0.53	2.88 \pm 0.80	2.68 \pm 0.72	2.59 \pm 0.51

\bar{X} : Mean, SD: Standard deviation, Min: Minimum, Max: Maximum

No significant differences were detected in mean scores for health communication problems among individuals with epilepsy by sex, health expenditure, seizure type, or seizure characteristics ($p > 0.05$). However, the mean scores for effective communication problems ($t = 2.718$, $p < 0.01$) and social communication problems ($t = 3.817$, $p < 0.001$) differed significantly by marital status, with married individuals showing higher scores than single individuals.

By educational status, the mean score for social communication problems differed significantly ($F = 6.848$, $p < 0.001$): primary school graduates had higher scores than illiterate individuals, and primary and secondary school graduates had higher scores than those with a bachelor's degree or higher. No significant differences were observed in effective communication problems or communication barriers across educational levels.

Place of residence showed a significant effect on social communication problems ($F = 3.352$, $p < 0.05$); however, multiple-comparison tests revealed no significant differences between specific groups.

Employment status significantly affected social communication problem scores ($t = 2.229$, $p < 0.05$), with unemployed individuals reporting higher scores than employed individuals.

Perceived income status was significantly associated with effective communication problems ($t = 3.513$, $p < 0.001$), with participants whose income was less than their expenses having higher scores.

Finally, drug use influenced problems with effective communication ($t = -2.288$, $p < 0.05$), such that polytherapy users reported higher scores than monotherapy users (Table 2).

DISCUSSION

Effective communication between individuals with epilepsy, their families, and healthcare professionals is crucial for optimal treatment and care management. Previous studies have emphasized the negative impact of communication problems on treatment outcomes.²⁷ Improving communication is key to enhancing the quality of healthcare for these patients.^{28,29} The results of the present study, which examined healthcare communication problems among individuals with epilepsy, are discussed in the context of existing literature.

This study aimed to investigate the health communication challenges faced by individuals with epilepsy and the factors influencing these difficulties. The main findings revealed that married individuals, individuals with higher levels of education, unemployed individuals, and low-income patients experienced more pronounced communication problems.

Furthermore, patients receiving polytherapy exhibited greater communication difficulties than patients receiving monotherapy. These results highlight the influence of demographic, socioeconomic, and treatment-related factors on patient-provider communication and underscore the need for targeted interventions to improve care quality, patient satisfaction, and overall health outcomes in individuals with epilepsy.

The study found that married individuals experienced more problems with effective and social communication than single individuals.²⁷ However, some studies report contrasting findings, indicating either no significant relationship between marital status and communication problems³⁰ or that single individuals face more social communication challenges.³¹ This discrepancy may reflect differences in study populations, cultural contexts, or social support systems. In our cohort, married individuals may experience reduced social tolerance because of responsibilities, which highlights the importance of individual and contextual factors when interpreting the results.

Notably, the study found that individuals with higher levels of education reported more communication problems in healthcare settings. Consistent with previous research, this may result from increased expectations and attention to detail during healthcare interactions.^{27,30-34} Conversely, patients with lower education levels may prefer sincere and empathetic communication styles, facilitating clearer and more effective interactions with healthcare professionals. Thus, more highly educated individuals may perceive communication challenges more acutely, while individuals with less education may experience fewer problems due to simpler, more direct communication styles. Unemployed individuals with epilepsy experienced more social communication problems than employed individuals with epilepsy. No comparable findings regarding employment status were identified in the literature. This may reflect narrower social circles, psychosocial stress, economic concerns, or social perceptions affecting communication among unemployed patients. Low-income individuals experienced more pronounced communication difficulties, consistent with findings that limited social support can hinder effective health communication.³⁵ The literature shows mixed results; some studies report that higher-income individuals face more social communication problems,³² while others find no relationship between income and communication challenges.^{30,32,36} In our study, low-income patients may hesitate to express their needs due to limited social support networks. Although differences in social communication problems were observed between places of residence, multiple-comparison tests showed that these differences were not statistically significant. This suggests that residence alone does not directly affect social communication, and other individual or socioeconomic factors may play a larger role.³³ Polytherapy users had higher scores for communication problems than monotherapy users, indicating that

Table 2. Comparison of mean scores of epilepsy patients in health communication

				Health communication problems scale					
				The problem of effective communication		Social communication problem		Communication barriers	
Personal data		n	%	Mean	SD	Mean	SD	Mean	SD
Sex	Female	97	56.4	2.40	0.51	2.97	0.72	2.66	0.68
	Male	75	43.6	2.41	0.56	2.76	0.88	2.71	0.77
Test and significance				t=-0.116 ^a , p=0.908		t=1.748 ^a , p=0.082		t=-0.444 ^a , p=0.657	
Marital status	Married	106	61.6	2.49	0.55	3.07	0.67	2.70	0.72
	Single	66	38.4	2.27	0.48	2.58	0.89	2.64	0.73
Test and significance				t=2.718 ^a , p= 0.007		t=3.817 ^a , p= 0.001		t=0.552 ^a , p=0.581	
Education get status	Literate or literate	17	9.9	2.35	0.55	2.61	0.75	2.62	0.76
	Primary education	41	23.8	2.59	0.64	3.20	0.71	2.65	0.85
	Secondary education	79	45.9	2.39	0.46	2.96	0.76	2.77	0.60
	Bachelor's degree and above	35	20.3	2.27	0.50	2.47	0.82	2.54	0.80
Test and significance				F=2.643 ^b , p=0.051		F=6.848 ^b , p= 0.001		F=0.891 ^b , p=0.447	
Significant difference				-		1-2, 2-4, 3-4		-	
Residence	City	85	49.4	2.37	0.56	2.74	0.78	2.62	0.73
	District	71	41.3	2.43	0.49	2.97	0.81	2.77	0.68
	Village	16	9.3	2.51	0.58	3.23	0.71	2.58	0.85
Test and significance				F=0.558 ^b , p=0.574		F=3.352 ^b , p= 0.037		F=1.087 ^b , p=0.340	
Significant difference				-		-		-	
Working status	Working	115	66.9	2.36	0.55	2.69	0.88	2.72	0.78
	Not working	57	33.1	2.43	0.53	2.97	0.74	2.66	0.70
Test and significance				t=0.834 ^a , p=0.405		t=2.229 ^a , p= 0.027		t=-0.517 ^a , p=0.606	
Perceived income status	Income less than expenses	99	57.6	2.53	0.51	2.94	0.80	2.71	0.77
	Income equals expenses or exceeds income	73	42.4	2.25	0.52	2.80	0.78	2.64	0.66
Test and significance				t=3.513 ^a , p= 0.001		t=1.144 ^a , p=0.254		t=0.597 ^a , p=0.551	
Seizure frequency	Once in 1-3 months	55	32.0	2.55	0.57	2.95	0.82	2.69	0.73
	Once in 4-6 months	37	21.5	2.40	0.49	2.77	0.88	2.80	0.78
	Once in 7-12 months	17	9.9	2.47	0.32	3.02	0.62	2.97	0.62
	Once in 1-2 year(s)	63	33.7	2.28	0.55	2.84	0.78	2.52	0.68
Test and significance				F=2.618 ^b , p=0.053		F=0.584 ^b , p=0.626		F=2.371 ^b , p=0.072	
Significant difference				-		-		-	
Seizure types	Generalized tonic-clonic	73	42.4	2.47	0.53	3.01	0.77	2.64	0.79
	Partial	12	7.0	2.63	0.55	2.83	0.81	2.69	0.65
	Unidentified	87	50.6	2.32	0.52	2.77	0.81	2.71	0.68
Test and significance				F=2.749 ^b , p=0.067		F=1.843 ^b , p=0.161		F=0.151 ^b , p=0.860	
Significant difference				-		-		-	
Seizure awareness	Yes	37	21.5	2.44	0.57	2.67	0.89	2.51	0.76
	No	135	78.5	2.40	0.53	2.94	0.76	2.72	0.71
Test and significance				t=0.430 ^a , p=0.668		50.6		t=-1.578 ^a , p=0.116	
Medication	Monotherapy	86		2.32	0.58	2.80	0.87	2.68	0.73
	Polytherapy	86		2.50	0.47	2.96	0.71	2.67	0.72
Test and significance				=-2.288 ^a , p= 0.023		t=-1.281 ^a , p=0.202		t=0.079 ^a , p=0.937	

Significant findings are in bold, ^a: Independent groups t-test, ^b: One-way ANOVA test, SD: Standard deviation

multiple medications may contribute to communication difficulties through physical or cognitive impairments, such as confusion.^{37,38} These individuals may seek more guidance from healthcare personnel, highlighting the importance of effective and continuous communication to reduce polypharmacy complications.³⁹ Health communication plays a crucial role in healthcare effectiveness. Health is not only a biomedical concept but also a multidimensional phenomenon encompassing social, psychological, and cultural dimensions.⁴⁰

In the present study, the lowest mean score on the HCPS was 2.41 ± 0.53 in the effective communication sub-dimension, with an overall mean of 2.59 ± 0.51 . Compared with the literature reporting an overall mean of 2.79,³² our cohort experienced relatively fewer communication problems. This may reflect higher treatment adherence, frequent interactions with healthcare personnel, or specific sociodemographic characteristics.

Study Limitations

This study has several limitations. First, it was limited to individuals attending neurology outpatient clinics in the northern and eastern regions of Türkiye, which may limit generalizability. Second, data were self-reported, introducing potential social desirability bias. Third, the cross-sectional design prevents causal inference. Finally, variables such as psychiatric comorbidities, disease duration, and treatment compliance, which may affect communication, were not included. These limitations should be considered when interpreting and generalizing the findings.

CONCLUSION

Individuals with epilepsy experience moderate difficulties in health communication. Marital status, higher education, unemployment, low-income, and polytherapy use were associated with greater communication challenges. Future research should explore strategies to alleviate these problems and support effective communication. Healthcare professionals play a key role in educating patients about communication challenges. Educational programs should be developed to strengthen healthcare providers' communication skills. Clear informational materials and support groups for individuals with epilepsy should be established. Improving patients' communication skills can enhance their understanding of health issues and improve their quality of life and psychosocial well-being. Addressing individual needs and leveraging technology can optimize the benefits of health services for individuals with epilepsy.

Ethics

Ethics Committee Approval: Written approval was obtained from the Atatürk University Clinical Research Ethics Committee (approval no: 41, date: 26.01.2023).

Informed Consent: Verbal and written informed consent was obtained from individuals with epilepsy prior to data collection.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.B., D.A.C., N.İ.A., Concept: D.A.C., Design: D.A.C., Data Collection or Processing: D.A.C., N.İ.A., Analysis or Interpretation: D.A.C., Literature Search: N.B., D.A.C., Writing: N.B., D.A.C.

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

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The Effect of Neurology Rotation on Medical Students' Knowledge About Epilepsy and Attitudes Toward Disease

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Abstract

Objective: Negative attitudes toward epilepsy remain a common social or personal challenges for individuals with epilepsy. Limited knowledge levels and misconceptions are the main factors underlying stigmatization. This study aimed to evaluate the effects of neurology rotation on medical students' knowledge about epilepsy, approach to acute seizures, and attitudes toward epilepsy. The influence of epilepsy-related knowledge on attitudes toward the disease was also examined.

Methods: A total of 116 fifth-year medical students were included in the study and assessed twice: on the first day of the neurology rotation (pre-test) and on the final day of the 3-week rotation (post-test). All assessments were administered online using the “knowledge about epilepsy”, “approach to epileptic seizure” and “attitudes toward epilepsy” questionnaires. Pre-post changes in total scores were analyzed, and regression analysis was used to identify factors associated with attitudes.

Results: Students' total knowledge scores increased significantly following the rotation ($p=0.001$). In contrast, no significant difference was observed in total attitudes score between pre-test and post-test ($p=0.202$). Regression analysis demonstrated that higher knowledge levels and male gender were independently associated with more positive attitudes toward epilepsy.

Conclusion: The neurology rotation resulted in a significant improvement in medical students' knowledge about epilepsy; however, it did not lead to measurable changes in attitudes. These findings indicate that additional or alternative educational strategies may be necessary to influence attitudes toward epilepsy.

Keywords: Epilepsy, knowledge, attitudes, neurology rotation, medical student

INTRODUCTION

Epilepsy is a prevalent neurological disorder that is often manageable with antiepileptic medications. However, negative attitudes and stigma toward the disease remain a major social and personal burden.¹ In particular, limited knowledge and persistent misconceptions are key contributors to stigmatization, which has been shown to negatively affect the quality of life of patients with epilepsy.¹⁻³ Stigma is associated with multifactorial factors, inadequate education and insufficient disease-specific knowledge.⁴⁻⁹

Studies from many low- and middle-income countries indicate that misconceptions—such as viewing epilepsy as a psychiatric, spiritual, or supernatural condition—remain widespread. Historically rooted misbeliefs have contributed to social isolation, reduced access to education and employment, marital difficulties, and even mortality.¹⁰⁻¹⁴

Healthcare professionals play a crucial role in providing appropriate acute and long-term care for patient with epilepsy. As future physicians, medical students will frequently encounter patients with epilepsy, and their knowledge and attitudes directly influence the quality of care they provide. However, medical students themselves may hold misconceptions or negative beliefs that affect clinical decision-making.¹⁵⁻¹⁶ Structured educational interventions have been shown to reduce stigma and false beliefs.^{15,17-21}

This study had two primary objectives: (1) to assess fifth-year medical students' knowledge of epilepsy and their attitudes toward the disease; (2) to evaluate the impact of the neurology rotation on these parameters.

METHODS

Study Design and Participants

This prospective observational study was conducted among 5th-year medical students at Selçuk University Faculty of Medicine between January 2025 and June 2025. A total of 148 students were eligible to participate in the study. Of these, 116 students completed both assessments (pre-test and post-test) and were included in the final analyses. Students who did not complete either assessment or who submitted incomplete questionnaires were excluded (n=32).

All students underwent a 3-week neurology rotation, and assessments were conducted on the first day (pre-test) and the last day (post-test) of the rotation.

Ethical Considerations

The study received approval from the Selçuk University Local Ethics Committee (approval no: 2025/27, date: 16.01.2025). Participants were voluntary, and electronic informed consent forms were obtained. Data were collected via Google Forms and stored securely.

Neurology Rotation Structure

The neurology rotation lasts 3 weeks and includes theoretical lectures, bedside clinical training, outpatient clinic participation, case discussions, neurophysiology laboratory exposure, and intensive care unit observations. Epilepsy was covered in both theoretical and practical components; however, no structured education was provided on its social aspects. Epilepsy-related theoretical instruction totalled approximately 4 hours and included epidemiology, seizure types, diagnostic strategies, treatment modalities (medical and surgical), and seizure first-aid. During the rotation, students also participate in diagnosis and treatment of epilepsy under the supervision of neurologists.

Data Collection Tools

Five tools were administered twice (pre-test and post-test):

1. Demographic Form

Participants were questioned about their demographic characteristics: age, gender, marital status, number of siblings, place of residence (with family-alone-student house-dormitory) and family financial status. Additionally, inquiries were made about possession of a driver's license and active driving status.

MAIN POINTS

- Neurology rotation contributes to knowledge about epilepsy in medical students.
- The most inadequate knowledges about seizure are position and trying to open mouth.
- The most negative attitudes are dating or marriage with an epileptic patient.
- The knowledge about driving in epilepsy increases after neurology rotation.
- Male gender and higher knowledge level are associated with positive attitudes.

Furthermore, participants were questioned in medical history about neurological disease, epilepsy, antiepileptic drug, syncope and/or seizure. Finally, medical history about epilepsy in relatives, epilepsy among close friends, and witnessing of epileptic seizures were questioned.

2. Epilepsy Knowledge Questionnaire

The “epilepsy knowledge questionnaire” was employed to assess the participants' knowledge about epilepsy. The scale consists of a total of 16 items. This questionnaire includes items about social, medical, and seizure-related knowledge about epilepsy. All questions had closed-ended answers. Participants were asked to choose one of the following options: “true,” “no idea,” or “false”. Correct answers were scored as 1 point, while incorrect or “no idea” responses were scored as 0 points. The total score ranges from 0 to 16. An increased score indicates a higher level of knowledge about epilepsy. The scale is valid and reliable (Kuder Richardson =0.72).^{22,23}

3. Single-item Driving in Epilepsy Knowledge Question

An item was questioned to measure the participants' knowledge about driving in epilepsy. The legal driver's license regulation for epilepsy in Türkiye was updated on September 29, 2021.²⁴ Patients who have one of the following two items are evaluated by 3 neurologists. As a result, patients can obtain a driver's license.

3.a. A patient who has epileptic seizures—with or without loss of consciousness, provoked or unprovoked seizure—can obtain a driver's license under this condition. “If he/she does not have a seizure during the neurological follow-up at six-month intervals for three years (without antiepileptic medication or with maximum of two medications).”

3.b. Patients who have had one unprovoked epileptic seizure can get a driver's license under this condition. “Neurological follow-up at six-month intervals for two years, (no seizures and no antiepileptic medication for this period).”

4. Acute Seizure First-aid Knowledge Questionnaire

After literature review, the researchers developed a questionnaire to measure the students' knowledge and awareness about approach to acute epileptic seizures. The form consists of 7 items with answers as (yes, no or no idea). Frequencies and percentages of correct answers were calculated. For the items assessing approach to seizures with options “yes,” “no,” or “no idea,” correct responses were assigned 1 point, and incorrect or “no idea” responses received 0 points.^{25,26} This questionnaire is newly developed and not yet validity.

5. Attitudes Toward Epilepsy Scale

The “attitudes toward epilepsy” scale was used to assess the participants' attitudes toward epilepsy. This scale consists of 14 questions. The items are scored from 1 to 5 (five-point Likert scale; scores range from 1-completely disagree to 5-completely agree). The total score ranges from 0 to 70. Higher scores indicated more negative attitudes. The scale is valid and reliable (Cronbach's alpha =0.84).²²

Statistical Analysis

Analyses were performed using SPSS 26.0. Descriptive statistics included frequency, percentage, mean±standard deviation. Normality was assessed using Kolmogorov-Smirnov tests, histograms, and Q-Q plots. Chi-square was used for categorical variables. This analysis was used not only to describe frequency distributions, but specifically to compare categorical variables between groups (e.g., pre- and post-rotation knowledge levels, gender differences). Other statistical tests were applied as: McNemar or marginal homogeneity tests were used for paired categorical data; paired t-tests for normally distributed paired numerical variables; Pearson or Spearman correlation analyses as appropriate; and linear regression to identify predictors of attitudes. $P < 0.05$ was considered statistically significant.

RESULTS

Sociodemographic Characteristics

A total of 116 medical students completed both assessments before and after the neurology rotation. The mean age was 22.97 ± 0.88 years, and gender distribution was balanced (52.6% female; 47.4% male). Most participants lived with family, and 85.3% had a driver's license, although only 44% were active drivers. Additional demographic characteristics are summarized in Table 1.

Knowledge About Epilepsy

Overall epilepsy knowledge improved significantly following the rotation. The mean total knowledge score increased from 13.43 ± 1.92 to 15.00 ± 1.17 ($p = 0.001$). Seven of the sixteen items showed statistically significant improvement; these are detailed in Table 2A. Before the rotation, participants had sufficient knowledge about seizure triggers and misconceptions; however, knowledge about surgical treatment and seizure-related safety was limited. After the rotation, most items showed improvement, although some misconceptions persisted. The item-level results are shown in Table 2A.

Driving Regulations Related to Epilepsy

Knowledge about driving eligibility in patient with epilepsy improved significantly after the rotation ($p = 0.017$). Driving knowledge level did not differ between participants with and without a driver's license ($p = 0.092$). Related findings are presented in Table 2B.

First-aid Knowledge for Epileptic Seizures

Four of seven first-aid items showed significant improvement after the rotation ($p < 0.05$). Although students demonstrated strong understanding of removing harmful objects and avoiding inappropriate resuscitation attempts, several misconceptions remained prevalent particularly regarding positioning the patient on their back and attempting to restrain convulsive movements. Detailed item responses are provided in Table 2C.

Attitudes Toward Epilepsy

Attitudes toward epilepsy did not change significantly after the rotation (pre-rotation: 22.27 ± 6.11 , post-rotation: 21.62 ± 6.11 , $p = 0.202$). Items about attitudes, there was no statistical difference

between the pre- and post-rotation groups ($p > 0.05$). However, attitudes about marriage remained less positive in post-rotation period ($p = 0.027$). All attitude-related results are shown in Table 3.

Correlation Between Knowledge and Attitudes

In the pre-rotation assessment, knowledge about epilepsy and attitudes toward disease were not significantly correlated ($r = -0.089$; $p = 0.342$). After the rotation, a statistically significant

Table 1. Sociodemographic characteristics of fifth year medical students

Variables	Overall (%), n=116*
Gender	
Female	61 (52.6)
Male	55 (47.4)
Financial situation in family**	
Under and national minimum wage	15 (12.9)
More than national minimum wage	101 (87.1)
Marital status	
Married	1 (0.9)
Single	115 (99.1)
Brothers/sisters	
Yes	112 (96.6)
No	4 (3.4)
Neurological diseases in history	
Yes	4 (3.4)
No	112 (96.6)
Syncope and/or seizure in history	
Yes	25 (21.6)
No	91 (78.4)
Epilepsy in history	
Yes	1 (0.9)
No	115 (99.1)
Antiepileptic treatment in history	
Yes	1 (0.9)
No	115 (99.1)
Epilepsy in a first-degree relative	
Yes	3 (2.6)
No	113 (97.4)
Epilepsy in a second-degree relative	
Yes	13 (11.2)
No	103 (88.8)
Epilepsy in a close friend	
Yes	14 (12.1)
No	102 (87.9)
Witnessing to an epileptic seizure	
Before rotation	30 (25.9)
During rotation	12 (10.3)
No	74 (63.8)

*: Descriptive statistical methods were used to express as number (n) and percentages (%). A total of 116 participants were evaluated twice, before and after the rotation.

** : The current minimum wage in Türkiye is 26,005.50 (Turkish lira) 12 per month in 2025. It became valid on January 1, 2025. On January 1, 2025, 1 euro =36.46 Turkish liras

negative correlation was detected ($r=-0.214$; $p=0.021$), indicating that higher knowledge scores were associated with more positive attitudes. As a result of, in the post-rotation period, the attitudes score decreases and attitudes become more positive.

Predictors of Attitudes Toward Epilepsy

A multiple linear regression model identified predictors of post-rotation attitude scores. Female gender predicted more negative attitude ($\beta=0.327$; $p=0.001$). Higher knowledge scores predicted more positive attitudes ($\beta=-0.249$; $p=0.005$). Regression details are presented in Table 4.

DISCUSSION

Over the past decade, many studies have examined the pathophysiology, etiology, and treatment of epilepsy. Despite these advances, inadequate and incorrect knowledge, negative attitudes, and persistent misconceptions remain widespread. Patients with epilepsy may experience social stigma and discrimination throughout their lives, and negative attitudes about epilepsy have also been documented among healthcare professionals and

medical students.³⁻⁷ In this study, we aimed to evaluate whether a 3-week clinical neurology rotation contributed to improving epilepsy-related knowledge and students' attitudes. The rotation led to increased epilepsy-related knowledge; however, attitudes toward epilepsy did not change significantly. Regression analysis suggested that higher knowledge levels were associated with positive attitudes, particularly among male participants. Although higher knowledge levels were generally associated with more positive attitudes, this relationship was not observed among female students. One possibility is that attitudes in this group may be influenced more by personal beliefs, social factors, or prior experiences rather than short-term knowledge gains. Because our study was observational and not designed to explore gender-specific mechanisms, these interpretations remain speculative and should be investigated in future research.

Educational program play an important role in improving epilepsy-related knowledge.²⁷ Most previous studies have been cross-sectional and non-interventional design.²⁸⁻³⁰ Nevertheless, many have reported significant increases in knowledge following seminars, conferences, and structured training programs.³¹⁻³³ Some studies have also shown that knowledge and positive

Table 2. Knowledge about epilepsy and approach to acute epileptic seizure in medical students: pre-rotation and post-rotation period

		Pre-rotation group (n=116) ^A	Post-rotation group (n=116) ^B	p-value p ^{A-B}
A Items: Knowledge about epilepsy, n (%)				
Epilepsy is a neurological disease that has many types.	True	109 (94.0)	114 (98.3)	0.125*
Most people with epilepsy can work in suitable jobs.	True	112 (96.6)	114 (98.3)	0.687*
Most patients with epilepsy can be educated in public schools.	True	111 (95.7)	115 (99.1)	0.219*
Epileptic patients can be dangerous for other people during seizure.	False	65 (56.0)	75 (64.7)	0.123*
Some epileptic seizures may last for a few seconds.	True	98 (84.5)	115 (99.1)	0.001*
Epileptic seizures can be controlled with antiepileptic treatments in most patients.	True	99 (85.3)	110 (94.8)	0.007*
Brain surgical operation may be a curative treatment option for some patients with epilepsy.	True	47 (40.5)	97 (83.6)	0.001*
Most people with epilepsy have normal intelligence.	True	114 (98.3)	113 (97.4)	1.000*
Patients with epilepsy can be successful in working life.	True	112 (96.6)	114 (98.3)	0.687*
Abnormal neuronal activity in the brain is the main etiology for epileptic seizure.	True	103 (88.8)	114 (98.3)	0.003*
Epilepsy is an untreatable disease.	False	72 (62.1)	97 (83.6)	0.001*
Inadequate sleep, stress, and alcohol can induce seizures.	True	114 (98.3)	116 (100.0)	0.500*
When you witness a seizure, you can stop the seizure by smelling alcohol/cologne.	False	86 (74.1)	110 (94.8)	0.001*
Patients with epilepsy can have normal life like other people.	True	109 (94.0)	111 (95.7)	0.727*
Some types of seizures are difficult to recognize.	True	101 (87.1)	114 (98.3)	0.002*
When you witness a seizure, you should spill water on his/her face.	False	106 (91.4)	116 (100)	0.070*
B Items: Knowledge about driving in patients with epilepsy, n (%)				
Patients with epilepsy are not permitted to drive.	True	6 (5.2)	6 (5.2)	0.017**
I have got no information about driving in epilepsy.	True	49 (42.2)	28 (24.1)	
People with epilepsy can obtain a driving license, but there are some national legal regulations.	True	61 (52.6)	82 (70.7)	
C Items: Knowledge about approach to epileptic seizure, n (%)				
Restrain the patient. Try to hold the convulsive limbs.	False	73 (62.9)	93 (80.2)	0.005*
Remove sharp objects from the area.	True	116 (100)	116 (100)	1.000*
Loosen any tight clothing: undo buttons around the neck, remove glasses.	True	111 (95.7)	113 (97.4)	0.687*
Lay the patient on his/her back to make the person more comfortable.	False	26 (22.4)	54 (46.6)	0.001*
Try to open the patient's mouth with a stick, cloth, etc.	False	61 (52.6)	97 (83.6)	0.001*
Try to stop the seizure quickly with oral antiepileptic drugs.	False	87 (75.0)	110 (94.8)	0.001*
Start to cardiopulmonary resuscitation immediately.	False	110 (94.8)	116 (100)	1.000*

*: McNemar's test, **: Marginal homogeneity test. Bold font indicates statistical significance, $p<0.001$ was demonstrated as $p=0.001$

Table 3. Responses to attitudes toward epilepsy in medical students: pre-rotation and post-rotation period

		Pre-rotation group (n=116) ^A	Post-rotation group (n=116) ^B	p-value p ^{A-B}
A Items: Attitudes toward epilepsy, n (%)				
If I had epilepsy, I would hide my disease.	Completely disagree or disagree	92 (79.3)	97 (83.6)	0.472*
If I knew that a friend had epilepsy, I would stay away from him/her.	Completely disagree or disagree	114 (98.3)	114 (98.3)	1.000*
I would date someone who has epilepsy.	Completely agree or agree	65 (56.0)	67 (57.8)	0.892*
I would object to working with someone who has epilepsy.	Completely disagree or disagree	108 (93.1)	107 (92.2)	1.000*
I would be embarrassed if someone had epilepsy in my family.	Completely disagree or disagree	116 (100)	114 (98.3)	0.500*
I would object to the marriage of my child with someone who has epilepsy.	Completely disagree or disagree	76 (65.5)	92 (79.3)	0.027*
I would marry someone who has epilepsy.	Completely agree or agree	65 (56.0)	67 (57.8)	0.892*
I would marry someone who has epilepsy.	Completely disagree or disagree	113 (97.4)	112 (96.6)	1.000*
If I knew that my doctor had epilepsy, I would not trust him/her.	Completely disagree or disagree	116 (100)	115 (99.1)	1.000*
If I knew someone had epilepsy, I would prefer to stay away from him/her.	Completely disagree or disagree	114 (98.3)	113 (97.4)	1.000*
Epilepsy is a shameful disease.	Completely disagree or disagree	114 (98.3)	113 (97.4)	1.000*
I would be uncomfortable if I had to work with someone who had epilepsy.	Completely agree or agree	107 (92.2)	112 (96.6)	0.267*
I would feel comfortable if I were to be in the same place with someone who has epilepsy.	Completely disagree or disagree	114 (98.3)	111 (95.7)	0.453*
I think patients with epilepsy are frightening.	Completely disagree or disagree	114 (98.3)	112 (96.6)	0.687*
I think patients with epilepsy are not physically attractive.	Completely disagree or disagree	114 (98.3)	112 (96.6)	0.687*
B Total attitude score toward epilepsy, mean±SD		22.27±6.11	21.62±6.11	0.202**

^A: McNemar's test, ^{**}: Paired samples t-test. SD: Standard deviation

Table 4. Results of multivariate linear regression (backward) analysis

	B (95% CI)	Beta	t	p
Constant	44.814 (30.996-58.633)	1	6.426	0.001
Gender (reference: male)	3.985 (1.878-6.093)	0.327	3.747	0.001
Total knowledge score about epilepsy, post-rotation score	-1.301 [(-2.202)-(-0.399)]	-0.249	2.859	0.005

R²: 0.168, p<0.001 was demonstrated as p=0.001. Bold font indicates statistical significance, CI: Confidence interval

attitudes may persist for up to one year after the intervention.²¹ In another study, students who received a 6-week intensive training program demonstrated higher levels of knowledge and more positive attitudes.³¹ Online epilepsy courses have additionally been associated with improvements in long-term knowledge and clinical practice.³⁴ Positive changes in attitudes have also been reported among university students following targeted educational activities.³⁵

In our study, knowledge scores increased after the rotation; however, the lowest-performing items involved safety during seizures and surgical treatment options (“epileptic patients can be dangerous for other people during a seizure”, false; “brain surgery may be a curative option for some patients”, true; and “epilepsy is an untreatable disease”, false). Attitude scores decreased slightly after the rotation, but this change was not statistically significant. The most negative attitudes were related to dating and marriage (“I would date someone who has epilepsy” and “I would marry someone who has epilepsy”). Similar findings have been reported previously, with the most persistent negative attitudes among university students concerning intimate relationships.^{20,35} Although misconceptions often contribute to negative attitudes,^{36,37} the regression analysis in our study identified male gender and higher knowledge as significant correlates with positive attitudes.

Misconceptions about first-aid in seizure remain a major global problem. Common false beliefs—such as the idea that smelling

alcohol or cologne, or splashing water on the face, can stop a seizure—persist in many populations.¹⁶ Some individuals incorrectly believe that cardiopulmonary resuscitation (CPR) should be initiated immediately during seizures, a misconception that may lead to inappropriate or harmful actions.²⁵ Another harmful misconception involves attempting to open the patient’s mouth using objects such as sticks or cloths. Educational programs have been shown to reduce such unsafe practices; in one study, the proportion of participants who attempted to open the patient’s mouth decreased from 64.4% to 13.7% after training.³⁸ Other studies among health students and professionals have reported high initial rates of this belief.^{6,39} In our study, the most accurately answered items regarding seizure management were “remove sharp objects from the area” (true) and “start CPR immediately” (false). The least accurate items were “lay the patient on his/her back” and “try to open the patient’s mouth with a stick/cloth”, although knowledge of these improved after the rotation. While the rotation contributed to better seizure-management knowledge, these findings indicate that short clinical exposure may be insufficient. Structured first-aid education specific to epileptic seizures should be integrated into the medical curriculum.

Driving plays an important role in independence and social functioning for individuals with epilepsy.⁴⁰ However, neurological conditions such as epilepsy may increase accident risk due to impaired consciousness or adverse effects of antiepileptic medications.⁴¹ Approximately one-third of patients continue to

experience seizures despite treatment,⁴² and a notable proportion continue driving despite uncontrolled seizures.⁴³ Although precise figures vary internationally, it is known that some individuals conceal their diagnosis to obtain a driving license. Driving regulations for epilepsy differ across countries.^{44,45} In Türkiye, updated driving regulations have been implemented since 2021. In previous studies with fifth-year medical students, correct responses regarding driving restrictions increased substantially after educational seminar.²⁰ In our study, correct responses regarding driving restrictions increased from 52.6% to 70.7% after the rotation, indicating improved awareness of medico-legal issues. Medical students will soon be responsible for issuing health reports and counselling patients, targeted training on the legal aspects of epilepsy is essential.

Strengths of the study: (1) The prospective design allowed evaluation of changes over time. (2) It is one of the few studies specifically assessing the impact of a neurology rotation. (3) The assessment covered general knowledge about epilepsy, its causes, seizure management, and students' personal experiences. Therefore, many parameters were evaluated. (4) The instruments used were valid, reliable, and previously applied to medical students. (5) The pre- and post-rotation assessments enabled examination of rotation-related changes in knowledge and attitudes.

Study Limitations

(1) The use of closed-ended items may have limited the depth of knowledge assessment. (2) This single-centre design restricts generalizability; multicentre studies are needed to better evaluate knowledge and attitudes. (3) Long-term retention of knowledge and attitudes could not be assessed, as evaluations were performed only pre- and post-rotation. (4) Potential response biases, including voluntary participation and social desirability effects, could not be ruled out. (5) The lack of blinding may have influenced participants' responses, as students were aware of the study's purpose.

CONCLUSION

This study demonstrated that higher epilepsy-related knowledge was associated with more positive attitudes among medical students. Although the neurology rotation significantly improved knowledge—particularly regarding seizure management and driving regulations—several misconceptions persisted. Despite these improvements, overall attitude scores did not change meaningfully after the rotation. These findings highlight the need for enhanced educational strategies within the medical curriculum to further strengthen students' understanding and attitudes toward epilepsy.

Ethics

Ethics Committee Approval: The study received approval from the Selçuk University Local Ethics Committee (approval no: 2025/27, date: 16.01.2025).

Informed Consent: Participants were voluntary, and electronic informed consent forms were obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.E., B.A.D., Ç.Ş., Ş.Ö., Concept: F.E., C.A., Design: F.E., B.A.D., Ş.Ö., Data Collection or Processing: F.E., C.A., G.E., B.A.D., Ç.Ş., Analysis or Interpretation: F.E., G.E., Ş.Ö., Literature Search: F.E., B.A.D., Writing: F.E., C.A., G.E., B.A.D., Ç.Ş., Ş.Ö.

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