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Predictive factors for drug resistance in adult lesional epilepsy: Evidence from a cross-sectional study

Yetişkin lezyonel epilepside ilaç direncini öngören faktörler: Kesitsel bir çalışmadan kanıtlar

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ABSTRACT

Aim: Lesional epilepsy accounts for a substantial proportion of epilepsy cases, with treatment outcomes varying according to lesion type. Identifying predictors of drug resistance is essential to guide management and surgical planning. This study evaluated clinical, radiological, and electroencephalographic (EEG) predictors of treatment response in adults with lesional epilepsy.

Materials and Methods: Medical records of patients ≥18 years with MRI (magnetic resonance imaging)-confirmed structural lesions and ≥1 year of antiepileptic drug (AED) therapy were retrospectively reviewed. Patients with psychogenic non-epileptic seizures, acute symptomatic seizures, non-adherence, or prior epilepsy surgery were excluded. Data included demographics, seizure type, AED regimen, MRI lesion features, and interictal EEG findings. Drug resistance was defined as failure of two appropriately chosen, well-tolerated AED regimens.

Results: Ninety-six patients (41 males, 45 females; mean age 42 years) were included. Encephalomalacia was the most frequent lesion (43%), followed by tumors (26%), malformations of cortical development (MCD) (8%), cystic lesions (6%), vascular malformations (6%), and mesial temporal sclerosis (5%). Drug resistance occurred in 26% of cases, with MCD showing the highest rate (62%, $p = 0.026$). Gender, age at onset, generalized motor seizures, EEG abnormalities, and lesion laterality were not significantly associated with drug resistance.

Conclusion: MCD is strongly associated with AED resistance in adults with lesional epilepsy, while other lesion types tend to respond more favorably. Early recognition of high-risk patients may facilitate timely surgical evaluation and improve seizure control outcomes.

Keywords: Lesional epilepsy, drug resistant epilepsy, epilepsy related cerebral lesions, malformations of cortical development, seizure prognosis

ÖZ

Amaç: *Lezyonel epilepsi, epilepsi olgularının önemli bir kısmını oluşturmakta olup tedavi yanıtı, lezyon tipi ve klinik özelliklere göre değişmektedir. Bu olgularda ilaç tedavisine dirence etki eden faktörlerin belirlenmesi, hasta yönetimi ve cerrahi operasyonların planlanmasında gereklidir. Bu çalışmanın amacı, erişkin lezyonel epilepsi hastalarında klinik, radyolojik ve elektroensefalografi (EEG) bulgularının ilaç tedavisinde elde edilen yanıt ile ilişkisini belirlemektir.*

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Gereç ve Yöntem: *MRG (magnetik rezonans görüntüleme) ile doğrulanmış yapısal lezyonu bulunan, ≥18 yaşında ve en az bir yıl süreyle antiepileptik ilaç (AEİ) tedavisi almış hastalar geriye dönük olarak incelendi. Psikojenik non-epileptik nöbet, akut semptomatik nöbet, tedaviye uyumsuzluk ve önceki epilepsi cerrahisi öyküsü olan hastalar dışlandı. Demografik veriler, nöbet tipi, AEİ rejimi, MRG lezyon özellikleri ve interiktal EEG bulguları kaydedildi. İlaç direnci, iki uygun ve iyi tolere edilen AEİ rejiminin başarısızlığı olarak tanımlandı.*

Bulgular: *Toplam 96 hasta (41 erkek, 45 kadın; ortalama yaş: 42 yıl) dahil edildi. En sık görülen lezyon ensefalomalazi (%43) olup, bunu tümörler (%26), kortikal gelişim malformasyonları (KGM) (%8), kistik lezyonlar (%6), vasküler malformasyonlar (%6) ve mezial temporal skleroz (%5) izledi. İlaç direnci %26 oranında görüldü; KGM grubunda bu oran %62 ile anlamlı olarak daha yüksekti (*p *= 0,026). Cinsiyet, nöbet başlangıç yaşı, jeneralize motor nöbet varlığı, EEG anormallikleri ve lezyon lateralitesi ile ilaç direnci arasında anlamlı ilişki bulunmadı.*

Sonuç: *KGM, erişkin lezyonel epilepsi hastalarında ilaç direnci ile güçlü şekilde ilişkilidir. Bu hastaların erken dönemde tanınması, cerrahi değerlendirme sürecinin hızlandırılmasını ve nöbet kontrolünün iyileştirilmesini sağlayabilir.*

Anahtar Sözcükler: *Lezyonel epilepsi, ilaç dirençli epilepsi, epilepsi ilişkili serebral lezyonlar, kortikal gelişim malformasyonları, nöbet prognozu*

INTRODUCTION

Epilepsy is the most common serious neurological disorder, affecting an estimated 50 million people worldwide (1). While the prognosis is generally favorable for many individuals, approximately one-third of patients continue to experience seizures despite appropriate antiepileptic drug (AED) therapy (2). Drug-resistant epilepsy is a major clinical challenge. Several factors have been proposed as predictors of poor treatment response. These include high seizure frequency, seizure clustering before treatment onset, psychiatric comorbidities, early age at onset, prolonged disease duration, lack of response to the first prescribed AED, and the presence of structural brain lesions on neuroimaging (2-9).

Structural etiologies are common in epilepsy, with Kwan and Brodie reporting that 29% of cases occur secondary to a structural lesion [2]. In this group, 43% of patients continued to have seizures after drug treatment, compared with 26% of those with idiopathic epilepsy. Among both pediatric and adult populations, the most frequent lesion-related causes include hippocampal sclerosis, cortical developmental malformations, and brain tumors. Identifying drug-resistant cases in this subgroup is crucial, as resective surgery can abolish or significantly reduce seizures in appropriately selected patients (10). Given the significant impact of drug resistance on patient outcomes, understanding the clinical, etiological, and electrographic predictors of treatment failure is essential. This study aims to investigate these factors in patients with lesional epilepsy to guide more effective treatment strategies and improve seizure control rates.

MATERIALS AND METHODS

This retrospective, cross-sectional observational study reviewed medical records of patients with lesional epilepsy who attended the epilepsy outpatient clinic over a two-year period. Eligible patients were ≥18 years old, had a structural lesion confirmed by cranial MRI, and had received AED therapy for at least one year. Patients were excluded if they had a history suggestive of psychogenic non-epileptic seizures, incomplete or unreliable records, acute symptomatic seizures, non-adherence to AED therapy, structural lesions deemed unrelated to epilepsy, or a history of epilepsy surgery.

Data collected included demographic characteristics (age, sex), age at epilepsy diagnosis, seizure type, AED regimen, seizure occurrence in the preceding six months, and cranial magnetic resonance imaging (MRI) and interictal electroencephalography (EEG) findings. Epilepsy was diagnosed according to the 2014 International League Against Epilepsy (ILAE) definition (11), and seizure types were classified using the 2025 updated classification of seizures ILAE system (12). All patients were followed for a minimum of six months. A good response to treatment was defined as a reduction in seizure frequency to fewer than three times the longest pretreatment inter-seizure interval or to fewer than one seizure per month—whichever was longer—

after an adequate AED trial (13,14). A poor response was defined as failure to meet these criteria despite adequate trials of two well-tolerated, appropriately selected AEDs, administered sequentially or in combination (13).

Cranial MRI examinations were performed using 1.5 T or 3 T scanners. Protocols included T1-weighted, T2-weighted, FLAIR (axial, coronal, sagittal), axial DWI/ADC, axial T2*/SWI, coronal IR, and post-contrast T1-weighted sequences, depending on lesion characteristics. Lesions were classified as cerebromalacic, mesial temporal sclerosis, cortical dysplasia, tumors, cystic lesions, vascular malformations, or atrophic lesions, and evaluated for laterality. Interictal scalp EEG recordings were obtained using the international 10–20 electrode placement system. Studies were conducted during wakefulness and or sleep, lasted approximately 20 minutes, and were analyzed for epileptiform discharges or continuous/proximal slow-wave activity (delta or theta range). Epileptiform discharges were defined as spikes (20–70 ms) or sharp waves (70–200 ms) (15).

Statistical Analysis

Quantitative variables were summarized as ranges and means, while qualitative variables were presented as frequencies and percentages. Categorical data were analyzed using the chi-squared test or Fisher's exact test, as appropriate. Pearson's correlation coefficient was applied to assess linear relationships. A p-value ≤ 0.05 was considered statistically significant. The study protocol (Date:22.08.2024, No: 24-8T/59) was reviewed and approved by the Ethical Committee of Ege University.

RESULTS

Ninety-six patients met the inclusion criteria, with a mean age of 42 years. Of these, 41 were female and 55 were male. 62 patients were diagnosed with epilepsy after the age of 18, while 34 patients received the diagnosis before adulthood. Among those diagnosed before 18 years, the age at diagnosis ranged from 1 to 17 years, with 17 patients diagnosed at or before the age of 5.

All patients experienced focal seizures, either preserved or impaired consciousness, and 64 patients also presented with generalized tonic clonic seizures (GTCS) accompanied by focal seizures. Regarding AED therapy, 61 patients were managed with monotherapy, 20 with dual therapy, and 15 with polytherapy involving three or more agents. Seizure control was achieved in 71 patients (74%), whereas 25 patients (26%) continued to experience seizures despite treatment.

MRI revealed encephalomalacic lesions as the most frequent structural abnormality (n = 41), followed by tumors (n = 25), malformations of cortical development (MCD) (n = 8), cystic lesions (n = 6), vascular malformations (n = 6), mesial temporal sclerosis (n = 5), and atrophic lesions (n = 2). In three patients, lesion type could not be determined. Figure 1 presents the etiological distribution of MRI findings.

Encephalomalacic lesions occurred in 45% of patients diagnosed after age 18 and 41% of those diagnosed earlier. Tumoral lesions were identified in 29% and 21% of these groups, respectively. Overall, lesion distribution did not differ significantly between the two age groups (chi-square, p =0,255), except for cystic lesions, which were significantly more frequent in patients diagnosed before age 18 (Fisher's exact test, p =0.020).

Analysis of lesion laterality revealed that left hemispheric involvement (42%) was more common than right hemispheric lesions (33%), and 17% of patients had bilateral lesions. Interictal EEG was available for 93 patients. 64 recordings were obtained during wakefulness only, while 29 were acquired during both wakefulness and sleep. Pathological EEG findings were observed in 65% of patients (Table 1), with epileptiform discharges present in 47% of cases and slow-wave abnormalities in 53% of cases.

Table-1. Comparison of the demographic features, clinical findings, EEG results

		Total (n=96)	Controlled seizures (seizure free at least 6 months) n= 71	Uncontrolled seizures (having seizures in 6 months) n=25	P value
Sex	female	41 (43%)	30 (73%)	11 (27%)	0,874
	male	55 (57%)	41(75%)	14 (25%)	
Age	mean	42	44	40	0.153
Age of onset	<18 years	34 (35%)	23 (68%)	11 (32%)	0,298
	⩾ 18 years	62 (65%)	48 (77%)	14 (23%)	
Type of seizure	Presence of generalized tonic clonic seizures	64 (67%)	50 (78%)	14 (22%)	0,609
EEG	Normal	31 (32%)	26 (84%)	5 (16%)	0.302
	Abnormal	62 (65%)	43 (69%)	19 (31%)	

chi-square test; p value>0.05, not statistically significant differences between variables.

In this study, neither gender, age at epilepsy onset (before or after 18 years), the presence of generalized tonic clonic seizures, nor pathological interictal EEG findings showed a significant association with poor response to AED therapy in patients with lesional epilepsy (chi-square test, p > 0.05) (Table 1). By contrast, lesion type demonstrated a notable impact on treatment outcomes. Malformations of cortical development were significantly more likely to be associated with drug-resistant epilepsy compared with other MRI-detected lesions (Fisher's exact test, p = 0.026), with approximately 62% of affected patients showing intractability to AEDs. Cystic lesions and mesial temporal sclerosis were the second and third most frequent causes of treatment resistance, respectively. In contrast, tumors, encephalomalacic lesions, and vascular malformations were associated with lower rates of intractability. Furthermore, lesion laterality—whether right- or left-hemispheric—did not have a statistically significant influence on drug resistance (chi-square test, p=0.430). Detailed MRI lesion characteristics are provided in Table-2.

Table-2. Comparison of MRI findings between controlled and poorly controlled patients

		Total (n=96)	Controlled (seizure free at least 6 months) n=71	Uncontrolled (having seizures in 6 months n=25	P value
Type of lesion	Cerebromalacic lesion	41 (43%)	33 (81%)	8 (19%)	0.850
	MTS	5 (5%)	3 (60%)	2 (40%)	0.465
	MCD	8 (8%)	3 (38%)	5 (62%)	0.026*
	Tumors	25 (26%)	19 (76%)	6 (24%)	0.745
	Cystic lesion	6 (6%)	3 (50%)	3 (50%)	0.356
	Vascular malformation	6 (6%)	5 (83%)	1 (17%)	0.705
	Atrophic lesion	2 (2%)	2 (100%)	0	0.560
Hemisphere involved	Right	32 (33%)	24 (75%)	8 (25%)	0.430
	Left	40 (42%)	30 (75%)	10 (25%)	
	Bilateral	16 (17%)	12 (75%)	4 (25%)	

MTS : Mesial temporal sclerosis, MCD: Malformation of cortical development. Statistically significant difference was observed in MCD in terms of drug resistancy of seizures. Fisher's Exact Test, p<0.05.

DISCUSSION

In this study, we sought to determine the factors influencing drug resistance in adults with lesional epilepsy. Previous literature has identified several cranial structural abnormalities commonly associated with epilepsy, including hippocampal sclerosis, MCD, tuberous sclerosis complex, low-grade gliomas, vascular malformations, and hypothalamic hamartomas (16). In our cohort, the most prevalent lesion type was encephalomalacia, followed by tumors, MCD, cystic lesions, vascular malformations, and mesial temporal sclerosis. The predominance of encephalomalacic lesions likely reflects the adult composition of our study population, as these lesions are most often sequelae of cerebral ischemia or hemorrhage. This pattern underscores the role of age-related cerebrovascular events in shaping the structural substrates of epilepsy in adults and may have implications for both prognosis and therapeutic response.

In our cohort, the majority of patients were drug responsive, with 25% identified as having drug-resistant epilepsy. This proportion was lower than that reported in previous study [2], which may be attributed to differences in patient age distribution and the prevalence of specific lesion types. While male patients have been reported to exhibit higher rates of lesional epilepsy than females, likely due to a greater risk of structural brain injury from trauma (17), no gender-related difference was observed in our series. This finding may be explained by the low frequency of traumatic brain injury in our cases.

In lesional epilepsies, an early age at seizure onset and the presence of abnormal EEG findings are frequently reported as predictors of poor response to AEDs (18). Early onset between 0 and 5 years has been significantly associated with drug resistance (19) possibly due to adaptive functional reorganization in brain regions distant from the lesion, reducing responsiveness to treatment (20). In the present study, age at epilepsy diagnosis was not associated with drug resistance, likely because most patients were diagnosed after 18 years of age, with only 18% diagnosed at or before 5 years. Although abnormal EEG findings have been reported as significant predictors of poor seizure control, there is no prospective evidence evaluating the prognostic value of interictal EEG after brain injury (21). Uva et al. (22) proposed that interictal spikes could play a causal role in ictogenesis when reaching a critical temporal density. In our cohort, pathological EEG findings were not associated with drug unresponsiveness. Slow-wave abnormalities were often related to MRI-detected lesions; however, interictal epileptiform discharges—more directly linked to epileptogenicity—were detected in only 29 cases. This limited detection may be due to the majority of EEGs being recorded in the awake state. Previous literature indicates that EEG during sleep increases diagnostic and prognostic yield, as latent interictal epileptiform discharges are frequently activated during non-rapid-eye-movement (NREM) sleep stages I and II, with focal discharges tending to become bilateral and generalized (23-26). The relatively short duration of routine EEG may also have limited epileptiform discharge detection. Burkholder et al. (27) reported a 19% increase in interictal epileptiform discharge detection when recording duration was extended from 30 to 60 minutes. Beyond technical considerations, physiological factors—including the size and location of the cortical generator, its orientation relative to electrodes, and the degree of neuronal synchrony—may influence detectability [28]. Furthermore, a study on lesional focal epilepsy found no statistically significant differences between patients with and without interictal discharges in terms of age, gender, epilepsy duration, seizure frequency, seizure focus location, epilepsy risk factors, or MRI lesion type (28).

The prognosis of epilepsy may be influenced by the predominant seizure type, particularly in patients exhibiting multiple seizure patterns. In our cohort, we focused on individuals with focal seizures and assessed whether the presence of GTCS might be associated with drug resistance. Our findings indicated that the coexistence of GTCS with focal preserved or impaired consciousness seizures did not significantly affect drug resistance. This observation aligns with the results of Mattson et al., who reported that in patients with lesional epilepsy, the most favorable response to AEDs occurred in those with GTCS, followed by patients with mixed seizure types (focal and generalized), while the least favorable outcomes were observed in individuals with only focal impaired consciousness seizures (29).

Our findings indicate that MCD are more frequently associated with drug-resistant epilepsy compared with other MRI-detected lesions, including tumors, cystic lesions, vascular abnormalities, and gliotic changes. This aligns with previous reports by Palmini et al. (30) and Semah et al. (31). A plausible explanation is that MCD may involve an epileptogenic network extending beyond the lesion visible on MRI, rendering it more resistant to AEDs than other structural causes, such as post-traumatic or post-infarction encephalomalacia (32). Although not statistically significant, our cohort also showed a higher prevalence of drug-resistant epilepsy in patients with mesial temporal sclerosis and cystic lesions. The predominant cystic pathologies were arachnoid and porencephalic cysts, with epilepsy onset occurring before 18 years of age. The relationship between arachnoid cysts and epilepsy remains controversial, as some studies report inconsistent findings (33). Nonetheless, cysts adjacent to epileptogenic regions—particularly within the temporal lobe—are more likely to be associated with seizures (34). Furthermore, the correlation between cyst location and clinico-electroencephalographic features has been emphasized in recent studies (34). Porencephalic cysts may present with diverse neurological manifestations, including epilepsy, with approximately 25% of cases being drug-resistant (35). In some cases, amygdalo-hippocampal atrophy may coexist (36), though this was not observed in our cohort. In our series, seizure semiology and EEG findings were concordant with the anatomical location of cystic lesions.

The potential role of lesion laterality related to epileptogenicity has been explored in previous literature, with right-hemispheric lesions reported to carry a higher epileptogenic potential in ischemic stroke (37) and brain tumors (38). However, the underlying mechanisms remain uncertain. In our study, we also examined whether lesion laterality on MRI might influence drug resistance. However, our findings did not reveal a significant association between lesion laterality and antiepileptic drug responsiveness in patients with lesional epilepsy.

A principal limitation of this study is its retrospective design, which inherently carries the risk of selection and information biases. Additionally, the relatively small sample size may reduce the statistical power and limit the generalizability of the results to broader patient populations.

CONCLUSION

This study highlights the association between specific structural brain abnormalities and drug resistance in lesional epilepsy, with MCD emerging as a significant predictor compared to other lesion types. Future prospective, multicenter studies with larger cohorts and standardized follow-up protocols are warranted to validate these findings and provide a more comprehensive understanding of drug resistance patterns in lesional epilepsy.

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References

1. Brodie MJ, Dichter MA. Antiepileptic drugs. N Engl J Med. 1996;334(3):168-175. doi:10.1056/NEJM199601183340308.
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med. 2000;342(5):314-319. doi:10.1056/NEJM200002033420503.
3. French JA. Refractory epilepsy: clinical overview. Epilepsia 2007;48(Suppl.1):3–7.
4. Camfield PR, Camfield CS. Antiepileptic drug therapy: when is epilepsy truly intractable? Epilepsia 1996;37(Suppl.1):S60–5.
5. French JA. Response to Early AED Therapy and Its Prognostic Implications. Epilepsy Curr. 2002;2(3):69-71. doi:10.1111/j.1535-7597.2002.00025.x.
6. Hitiris N, Mohanraj R, Norrie J, Sills GJ, Brodie MJ. Predictors of pharmacoresistant epilepsy. Epilepsy Res. 2007;75(2-3):192-196. doi:10.1016/j.eplepsyres.2007.06.003.

7. Kwan P, Brodie MJ. Drug treatment of epilepsy: when does it fail and how to optimize its use?. CNS Spectr. 2004;9(2):110-119. doi:10.1017/s1092852900008476.
8. Kwan P, Brodie MJ. Refractory epilepsy: a progressive, intractable but preventable condition?. Seizure. 2002;11(2):77-84. doi:10.1053/seiz.2002.0593.
9. Cendes F. Neuroimaging predictors of AED resistance in new-onset epilepsies. Epilepsia. 2011;52 Suppl 4:7-9. doi:10.1111/j.1528-1167.2011.03143.x.
10. Engel J Jr. Surgery for seizures. N Engl J Med. 1996;334(10):647-652. doi:10.1056/NEJM199603073341008.
11. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475-482. doi:10.1111/epi.12550.
12. Beniczky S, Trinka E, Wirrell E, Abdulla F, Al Baradie R, Alonso Vanegas M, et al. Updated classification of epileptic seizures: Position paper of the International League Against Epilepsy. Epilepsia. 2025;66(6):1804–1823. doi:10.1111/epi.18338.
13. Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Hauser WA, Mathern G, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia. 2010;51(6):1069–1077. doi:10.1111/j.1528-1167.2009.02397.x
14. Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M. Adherence to treatment in patients with epilepsy: associations with seizure control and illness beliefs. Seizure. 2006;15(7):504–8. doi:10.1016/j.seizure.2006.06.003.
15. Aminoff MJ. Electrodiagnosis in clinical neurology. Electrodiagnosis in clinical neurology. 2005.
16. Vattipally VR, Bronen RA. MR imaging of epilepsy: strategies for successful interpretation. Neuroimaging Clin N Am. 2004;14(3):349-372. doi:10.1016/j.nic.2004.04.002.
17. Christensen J, Kjeldsen MJ, Andersen H, Friis ML, Sidenius P. Gender differences in epilepsy. Epilepsia. 2005;46(6):956-960. doi:10.1111/j.1528-1167.2005.51204.x
18. Zaki MA, ElSherif LN & Shamloul RM. Assessment of the response to antiepileptic drugs in epileptic patients with structural lesion(s) on neuroimaging. Egypt J Neurol Psychiatry Neurosurg 2020;56:108. doi:10.1186/s41983-020-00243-7.
19. Alare K, Ogungbemi B, Fagbenro A, Adetunji B, Owonikoko O, Omoniyo T, et al. Drug resistance predictive utility of age of onset and cortical imaging abnormalities in epilepsy: a systematic review and meta-analysis. Egypt J Neurol Psychiatry Neurosurg 2024;60:5. doi:10.1186/s41983-023-00753-w
20. Doucet GE, Sharan A, Pustina D, Skidmore C, Sperling MR, Tracy JI. Early and late age of seizure onset have a differential impact on brain resting-state organization in temporal lobe epilepsy. Brain Topogr. 2015;28(1):113-126. doi:10.1007/s10548-014-0366-6.
21. Angeleri F, Majkowski J, Cacchiò G, Sobieszek A, D'Acunto S, Gesuita R, et al. Posttraumatic epilepsy risk factors: one-year prospective study after head injury. Epilepsia. 1999;40(9):1222-1230. doi:10.1111/j.1528-1157.1999.tb00850.x.
22. Uva L, Librizzi L, Wendling F, de Curtis M. Propagation dynamics of epileptiform activity acutely induced by bicuculline in the hippocampal-parahippocampal region of the isolated Guinea pig brain. Epilepsia. 2005;46(12):1914-1925. doi:10.1111/j.1528-1167.2005.00342.x.
23. Dinner DS. Effect of sleep on epilepsy. J Clin Neurophysiol. 2002;19(6):504-513. doi:10.1097/00004691-200212000-00003.
24. Sammaritano M, Gigli GL, Gotman J. Interictal spiking during wakefulness and sleep and the localization of foci in temporal lobe epilepsy. Neurology. 1991;41(2 (Pt 1)):290-297. doi:10.1212/wnl.41.2_part_1.290.
25. Malow BA, Lin X, Kushwaha R, Aldrich MS. Interictal spiking increases with sleep depth in temporal lobe epilepsy. Epilepsia. 1998;39(12):1309-1316. doi:10.1111/j.1528-1157.1998.tb01329.x.
26. Malow BA, Selwa LM, Ross D, Aldrich MS. Lateralizing value of interictal spikes on overnight sleep-EEG studies in temporal lobe epilepsy. Epilepsia.1999;40(11):1587-1592. doi:10.1111/j.1528-1157.1999.tb02044.x.
27. Burkholder DB, Britton JW, Rajasekaran V, Fabris RR, Cherian PJ, Kelly-Williams KM, et al. Routine vs extended outpatient EEG for the detection of interictal epileptiform discharges. Neurology. 2016;86(16):1524-1530. doi:10.1212/WNL.0000000000002592.

28. Basiri R, Shariatzadeh A, Wiebe S, Aghakhani Y. Focal epilepsy without interictal spikes on scalp EEG: A common finding of uncertain significance. Epilepsy Res. 2019;150:1-6. doi:10.1016/j.eplepsyres.2018.12.009.
29. Mattson RH, Cramer JA, Collins JF. Prognosis for total control of complex partial and secondarily generalized tonic–clonic seizures: Department of Veterans Affairs Epilepsy Cooperative Studies No. 118 and No. 264 Group. Neurology. 1996;47(1):68-76. doi:10.1212/WNL.47.1.68.
30. Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y, Andermann E, et al. Focal neuronal migration disorders and intractable partial epilepsy: a study of 30 patients. Ann Neurol. 1991;30(6):741-749. doi:10.1002/ana.410300602.
31. Semah F, Picot MC, Adam C, Broglin D, Arzimanoglou A, Bazin B, et al. Is the underlying cause of epilepsy a major prognostic factor for recurrence? Neurology. 1998;51(5):1256-1262. doi:10.1212/wnl.51.5.1256.
32. Park KM, Shin KJ, Ha SY, Park J, Kim SE, Kim SE. Response to antiepileptic drugs in partial epilepsy with structural lesions on MRI. *Clin Neurol Neurosurg.* 2014;123:64–68. doi:10.1016/j.clineuro.2014.04.029.
33. Arroyo S, Santamaria J. What is the relationship between arachnoid cysts and seizure foci? *Epilepsia.*1997;38(10):1098–1102. doi:10.1111/j.1528-1157.1997.tb01199.x.
34. Aydin S, Darko K, Detchou D, Barrie U. Arachnoid cysts and epilepsy: seizures and epileptogenesis. *Neurosurg Rev.* 2024;47(1):544. doi:10.1007/s10143-024-02826-x.
35. Volpe JJ. *Neurology of the Newborn.* Saunders; 2001.
36. Ho SS, Kuzniecky RI, Gilliam F, Faught E, Bebin M, Morawetz R. Congenital porencephaly: MR features and relationship to hippocampal sclerosis. *AJNR Am J Neuroradiol.* 1998;19(1):135–141.
37. Galovic M, Döhler N, Erdélyi-Canavese B, Felbecker A, Siebel P, Conrad J, et al. Prediction of late seizures after ischaemic stroke with a novel prognostic model [the SeLECT score]: a multivariable prediction model development and validation study. *Lancet Neurol.* 2018;17(2):143–152. doi:10.1016/S1474-4422(17)30404-0.
38. Lee JW, Wen PY, Hurwitz S, Black P, Kesari S, Drappatz J, et al. Morphological characteristics of brain tumors causing seizures. *Arch Neurol*. 2010;67(3):336–342. doi:10.1001/archneurol.2010.2.