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Dolna 17, Warsaw,
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+48 226 0 227 03
editorial_office@rsglobal.pl

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DRUG-RESISTANT EPILEPSY – CURRENT TREATMENT STRATEGIES AND FUTURE THERAPEUTIC PERSPECTIVES

Honorata Juniewicz *(Corresponding Author, Email: honorataj96@gmail.com)*
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0001-0060-992X

Zuzanna Kudlińska
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0003-4422-7784

Ryszard Łagowski
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0007-8441-054X

Julia Kosęda
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0008-7742-2814

Anna Jędrasiak
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0001-3739-2066

Jakub Piotrowski
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0007-8889-713X

Patryk Heryć
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0004-9121-2670

Karolina Kananowicz
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0009-1229-6797

Zofia Laska
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0009-0001-0326-8251

Marianna Latour
Pomeranian Medical University, Szczecin, Poland
ORCID ID: 0000-0002-2568-5080

ABSTRACT

Drug-resistant epilepsy is a chronic neurological disorder characterized by persistent seizures despite the use of appropriate pharmacotherapy. This condition significantly deteriorates patients' quality of life, in-creases the risk of psychiatric disorders, and contributes to more frequent hospitalizations. Despite consid-erable progress in the development of new generations of antiepileptic drugs, there remains a pressing need to explore innovative therapeutic strategies. This article presents treatment approaches including pharmacotherapy, neurostimulation techniques, and the use of surgical interventions in epilepsy manage-ment. Special attention is given to targeted therapies that take into account genetic, immunological, and metabolic mechanisms of epilepsy. Although these therapies hold the potential for treatment, their imple-mentation is associated with numerous challenges, high costs, and the necessity for procedural standardi-zation. The article emphasizes the need for interdisciplinary collaboration and further research to improve treatment efficacy for patients suffering from drug-resistant epilepsy.

KEYWORDS

Drug-Resistant Epilepsy, Epilepsy Treatment, Drug Resistant Epilepsy Treatment, Neurostimulation, Targeted Therapy In Epilepsy, Epilepsy Surgery, Gene Therapy Epilepsy, Inflammation And Seizures, Ketogenic Diet Epilepsy

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1. Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, typically unprovoked seizures. Epilepsy affects approximately 0.5–1% of the population in developed countries, which translates into a substantial proportion of individuals at risk for neurological and psychiatric complications as well as hospitalization due to seizures [1]. Despite the availability of numerous antiepileptic drugs, a portion of patients suffer from drug-resistant epilepsy, in which seizure control remains insufficient despite the use of two appropriately selected and well-tolerated medications [2]. Drug-resistant epilepsy is associated with a significant deterioration in quality of life. Patients frequently experience depressive symptoms, comorbid anxiety, social stigmatization, as well as occupational and educational difficulties. These symptoms are considerably less common in the population with well-controlled seizures [3].

This condition leads to increased healthcare costs, a higher rate of hospitalizations, and elevates the risk of epilepsy-related mortality[4]. In light of these realities, there is a growing need to explore new therapeutic strategies, ranging from optimizing pharmacotherapy regimens and applying neurostimulation and surgical methods, to innovative targeted therapies (genetic, metabolic, immunological), which remain under active investigation. The aim of this review is to provide a comprehensive overview of currently used therapeutic interventions, as well as approaches to personalized treatment[5, 6]

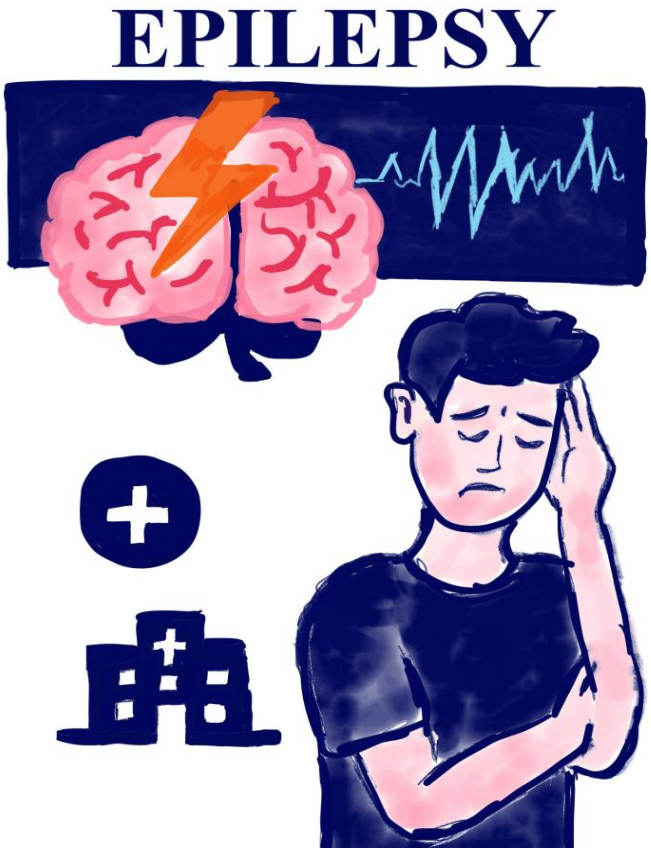

Fig. 1. *Epilepsy - chronic neurological disorder.*

2. Methodology

In order to prepare a literature review focused on current treatment methods for drug-resistant epilepsy, therapeutic strategies, and the perspectives of targeted therapy, sources from the PubMed database were analyzed. The review was conducted according to the following stages:

2.1. Source Selection

Included were original research articles as well as systematic reviews and meta-analyses published between 1994 and 2025.

2.2. Inclusion Criteria

Articles were included if they: -Addressed the topic of drug-resistant epilepsy in adults and children, in accordance with the definition of the International League Against Epilepsy (ILAE), -Described mechanisms of treatment resistance, -Concerned current forms of treatment: pharmacological, surgical, or neurostimulatory, -Contained information about targeted therapeutic methods currently under clinical investigation.

2.3. Content Analysis and Data Synthesis

The review directly utilized 40 publications. Data from the analyzed articles were grouped thematically and then described accordingly.

2.4. Methodological Limitations

-The data may be affected by methodological diversity and population heterogeneity.-Some of the discussed methods are still in preclinical or early clinical trial phases, which should be considered when interpreting the results.

3. Characteristics of Drug-Resistant Epilepsy

Drug-resistant epilepsy is a form of epilepsy in which seizures are not controlled despite the use of two appropriately selected and well-tolerated antiepileptic drugs. This definition has been adopted by the International League Against Epilepsy (ILAE)[2]. The mechanisms underlying resistance to treatment are complex and involve several hypotheses, including alterations in drug pharmacokinetics [7]. The most extensively studied mechanism is dysfunction of the blood–brain barrier (BBB), which leads to impaired transport of substances into the central nervous system. Disruptions in the BBB and increased permeability, resulting in weakened intercellular junctions and dysregulation of ion concentrations, have been observed in both clinical studies and animal models during the development of epilepsy [8]. Inflammatory factors also play a significant role by modifying the neuronal environment in ways that promote seizure generation[9]. The ILAE classification divides epilepsy into focal, generalized, epilepsy of unknown onset (either focal or generalized), and unclassified types. This classification takes into account the clinical presentation of seizures and EEG findings [10]. Furthermore, the ILAE classification emphasizes the importance of evaluating epilepsy etiologyand identifying comorbid conditions at each stage of classification. Epileptic syndromes are often age-dependent in their clinical manifestations [11]. The primary diagnostic tool used in drug-resistant epilepsy remains electroencephalography (EEG), which allows for the identification of seizure type and localization [12]. Magnetic resonance imaging (MRI) is a key imaging modality for detecting structural brain abnormalities, such as cortical dysplasia and hippocampal sclerosis, which are frequent causes of treatment resistance [13]. Neuropsychological assessments are essential for evaluating emotional and cognitive functions, quality of life in patients with DRE, and can also aid in lateralizing the epileptogenic focus[14].

4. Currently Used Therapeutic Strategies

4.1. Pharmacotherapy

Pharmacotherapy remains the primary method of epilepsy treatment. Both classical antiepileptic drugs, such as carbamazepine, valproate, and phenytoin, as well as newer-generation agents like lamotrigine, are commonly used. Despite their proven efficacy, some of these medications may cause mild adverse effects, including drowsiness, tremors, concentration difficulties, or gastrointestinal issues [15]. Treatment typically begins with monotherapy; if ineffective, combination therapy is considered. Despite the availability of numerous preparations, there is no single drug that is ideal for all patients. The choice of treatment depends on the type of epilepsy, comorbid conditions, patient age, and drug tolerance [16]. Newer-generation antiepileptic drugs, such as lamotrigine, are more often selected for elderly patients or those with comorbidities due to better tolerability [17].

Table 1. presents the mechanism of action of the drugs discussed above.

Table 1. Table presenting the mechanism of action of the drugs.

Medicament	Mechanism of Action
Carbamazepine	Blocks voltage-gated sodium channels in neurons, reducing their excitability and preventing excessive neuronal firing.
Valproate	Increases GABA levels and blocks sodium and calcium channels, helping stabilize brain activity.
Phenytoin	Acts by blocking voltage-dependent sodium channels, which suppresses excessive neuronal activity.
Lamotrigine	Blocks sodium channels and reduces the release of excitatory neurotransmitters such as glutamate. It stabilizes neuronal membranes.

4.2. Neurostimulation

Neurostimulation serves as an alternative treatment option for patients in whom pharmacotherapy alone fails to provide adequate seizure control. The three most commonly employed techniques are vagus nerve stimulation (VNS), deep brain stimulation (DBS), and responsive neurostimulation (RNS)[18].

VNS – Vagus Nerve Stimulation

This method involves the implantation of a device that cyclically delivers electrical impulses to the vagus nerve, located in the neck. The technique is generally well tolerated, with hoarseness and coughing being the most common side effects. In the majority of patients, a significant reduction in seizure frequency is achieved[19].

DBS – Deep Brain Stimulation

This technique entails the placement of electrodes in specific brain structures, most often the anterior nucleus of the thalamus. DBS is reserved for adults with severe drug-resistant epilepsy. In most cases, seizure frequency is significantly reduced; however, the procedure requires precise evaluation and specialized care[20].

RNS – Responsive Neurostimulation

RNS is one of the most advanced solutions currently available. The device detects epileptic activity in real time and responds by sending impulses that suppress the seizure. This leads to a substantial reduction in seizure frequency. The method is highly innovative and requires accurate localization of the epileptogenic focus[21]; [22].

4.3. Epilepsy Surgery

Surgical intervention is considered when pharmacological treatment and neuromodulation techniques fail to achieve seizure control. Surgical procedures are most commonly performed in patients with focal epilepsy, in which the seizure focus can be precisely localized within the brain [23]. The most frequently performed procedure is temporal lobectomy, which involves the resection of the temporal lobe where the epileptogenic focus is located[24]. Hemispherectomy, a procedure involving the functional disconnection or removal of one cerebral hemisphere, is sometimes employed in children with extensive brain abnormalities. Although these surgeries carry certain risks, their effectiveness can be very high. The majority of patients experience complete seizure freedom or a significant reduction in seizure frequency after surgery [25]. Postoperative complications, such as hydrocephalus or transient paresis, are rare and typically well managed. Most patients—especially children—adapt well after the surgery, including in terms of cognitive function [26].

5. Targeted Therapies – Emerging Treatment Approaches (In the preclinical stage or early clinical trials)

In recent years, researchers have increasingly focused on targeted therapies, which aim to tailor treatment to the specific mechanism causing the disease. As a result, therapy can become more effective while causing fewer side effects. Several new directions in epilepsy treatment are currently under development[27].

5.1. Gene and Molecular Therapies

Certain types of epilepsy have a genetic basis linked to mutations in specific genes. One of the best-studied genes is *SCN1A*, which encodes the NaV1.1 subunit. NaV1.1 is an ion channel that enables the conduction of electrical impulses in neurons. When a mutation occurs in this gene, it can lead to a rare and difficult-to-treat form of epilepsy known as Dravet syndrome. Scientists are testing new therapies that attempt to increase the production of NaV1.1 despite the presence of mutations by using antisense oligonucleotides. This approach has shown promising results in mice, improving brain function and reducing seizure frequency [28]. Another method is gene-silencing editing, which, instead of cutting DNA, activates gene expression to increase the production of the deficient protein. This strategy helps alleviate the symptoms of epilepsy [29].

5.2. Immunological Therapies

Neuroinflammation can significantly increase the risk of seizures. Researchers are exploring the potential of modulating the immune inflammatory response as a therapeutic strategy for epilepsy [30].

5.3. Metabolic Therapies and Diets

The ketogenic diet, used particularly in the treatment of pediatric epilepsy, involves consuming a very high amount of fats with minimal carbohydrate intake[31].

Its effects may be linked to the gut microbiota. In children following the ketogenic diet, changes in gut microbiota composition have been observed, potentially contributing to improved brain function[32]. Based on these findings, new approaches are being explored that aim to modulate the gut microbiome through ketogenic diets, probiotics, and fecal microbiota transplantation. It is important to emphasize that these methods are still under investigation and their future application may serve only as an adjunct to conventional antiepileptic therapies [33].

6. Prospects and Challenges in Targeted Therapies

The development of targeted epilepsy treatment holds great potential, but it also presents barriers that may limit its implementation. Personalizing treatment for a specific individual requires reliable biological markers to identify the underlying disease mechanism. A significant portion of current research involves heterogeneous patient groups, which further complicates the translation of findings into clinical practice [34]. Targeted therapies, especially those based on genetics or advanced technologies, are often highly expensive and require sophisticated laboratory infrastructure. These resources are lacking in many regions and countries, particularly where access to specialized care is limited. Assessing the effectiveness of treatment in diverse patient populations is only feasible through large-scale, coordinated multicenter studies, which ensure data reliability and allow for standardization of therapeutic approaches. Shared registries and international collaboration would enable the collection of meaningful data and facilitate the evaluation of treatment safety [35]. Artificial intelligence (AI) also demonstrates significant potential in the field of targeted therapy, especially in interpreting EEG results and seizure detection [36].

AI can be used to analyze imaging, genetic, and clinical data sets, enabling a more personalized approach to therapy. However, the actual implementation of such methods requires regulatory support, data protection, and the application of appropriate technical standards [37].

7. Discussion

Drug-resistant epilepsy remains a serious clinical challenge. Numerous studies show that traditional antiepileptic drugs do not always offer long-term seizure control in all patients, leading to reduced quality of life and increased hospitalizations [38].

In response to the limitations of traditional pharmacological approaches, increasing attention is being directed toward targeted therapies—those that consider individual patient factors, including genetic, metabolic, and immunological profiles. Such precision medicine strategies are opening new therapeutic avenues in the management of DRE. Promising results have been observed in studies involving gut microbiota modulation, immunological interventions, and gene-targeted therapies. Particularly noteworthy are approaches based on the identification of specific genetic mutations responsible for epilepsy, which may become direct therapeutic targets in the future. However, although these strategies appear highly promising, further clinical trials are necessary to establish their long-term safety and efficacy [39].

Given the complexity of drug-resistant epilepsy, an interdisciplinary approach is essential. Effective treatment requires collaboration not only among neurologists, but also geneticists, dietitians, immunologists, and experts in emerging technologies, including artificial intelligence. This integrated model of care enables the development of treatment plans tailored to the unique needs of each patient. Such collaborative practice facilitates faster and more accurate diagnosis, better identification of underlying disease mechanisms, and selection of the most appropriate therapeutic strategies. This personalized and multidisciplinary approach makes it possible to shift from symptomatic treatment toward etiological therapy, which, in the long term, may lead to a reduction in seizure frequency, improved patient quality of life, and decreased burden on healthcare systems. Nonetheless, continued research and implementation of innovative therapies in clinical practice remain essential to effectively address the needs of individuals living with drug-resistant epilepsy. [40]

Disclosure

Author contributions:

Conceptualization: Ryszard Łagowski, Marianna Latour
Methodology: Karolina Kananowicz, Zofia Laska
Software: Patryk Heryć, Honorata Juniewicz, Ryszard Łagowski
Validation: Patryk Heryć, Anna Jędrasiak
Formal analysis: Karolina Kananowicz, Jakub Piotrowski
Investigation: Marianna Latour, Zofia Laska, Zuzanna Kudlińska
Resources: Julia Kosęda, Ryszard Łagowski
Data curation: Julia Kosęda, Jakub Piotrowski
Writing – original draft: Anna Jędrasiak, Zuzanna Kudlińska
Writing – review & editing: Anna Jędrasiak, Marianna Latour
Visualization: Honorata Juniewicz, Patryk Heryć, Zofia Laska
Supervision: Karolina Kananowicz, Zuzanna Kudlińska, Honorata Juniewicz
Project administration: Julia Kosęda, Jakub Piotrowski

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In preparing this work, the authors used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed.

REFERENCES

1. Fiest, K. M., Sauro, K. M., Wiebe, S., Patten, S. B., Kwon, C., Dykeman, J., Pringsheim, T., Lorenzetti, D. L., & Jetté, N. (2016). Prevalence and incidence of epilepsy. *Neurology, 88*(3), 296–303. https://doi.org/10.1212/wnl.0000000000003509
2. Kwan, P., Arzimanoglou, A., Berg, A. T., Brodie, M. J., Hauser, W. A., Mathern, G., Moshé, S. L., Perucca, E., Wiebe, S., & French, J. (2009). Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia, 51*(6), 1069–1077. https://doi.org/10.1111/j.1528-1167.2009.02397.x
3. Akdemir, V., Sut, N., & Guldiken, B. (2016). Factors affecting the quality of life in drug-resistant epilepsy patients. *Acta Neurologica Belgica, 116*(4), 513–518. https://doi.org/10.1007/s13760-016-0622-5
4. Sultana, B., Panzini, M., Carpentier, A. V., Comtois, J., Rioux, B., Gore, G., Bauer, P. R., Kwon, C., Jetté, N., Josephson, C. B., & Keezer, M. R. (2021). Incidence and prevalence of drug-resistant epilepsy. *Neurology, 96*(17), 805–817. https://doi.org/10.1212/wnl.0000000000011839
5. Grinalds, M. S., Yoder, C., Krauss, Z., Chen, A. M., & Rhoney, D. H. (2022). Scoping review of rational polytherapy in patients with drug-resistant epilepsy. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 43*(1), 53–84. https://doi.org/10.1002/phar.2748
6. Jehi, L. (2024). Advances in therapy for refractory epilepsy. *Annual Review of Medicine.* https://doi.org/10.1146/annurev-med-050522-034458
7. Pérez-Pérez, D., Frías-Soria, C. L., & Rocha, L. (2019). Drug-resistant epilepsy: From multiple hypotheses to an integral explanation using preclinical resources. *Epilepsy & Behavior, 121,* 106430. https://doi.org/10.1016/j.yebeh.2019.07.031
8. Han, J., Wang, Y., Wei, P., Lu, D., & Shan, Y. (2024). Unveiling the hidden connection: The blood-brain barrier's role in epilepsy. *Frontiers in Neurology, 15.* https://doi.org/10.3389/fneur.2024.1413023
9. Zabrodskaya, Y., Paramonova, N., Litovchenko, A., Bazhanova, E., Gerasimov, A., Sitovskaya, D., Nezdorovina, V., Kravtsova, S., Malyshev, S., Skiteva, E., & Samochernykh, K. (2023). Neuroinflammatory dysfunction of the blood–brain barrier and basement membrane dysplasia play a role in the development of drug-resistant epilepsy. *International Journal of Molecular Sciences, 24*(16), 12689. https://doi.org/10.3390/ijms241612689
10. Beniczky, S., Trinka, E., Wirrell, E., Abdulla, F., Baradie, R. A., Vanegas, M. A., Auvin, S., Singh, M. B., Blumenfeld, H., Fressola, A. B., Caraballo, R., Carreno, M., Cendes, F., Charway, A., Cook, M., Craiu, D., Ezeala-Adikaibe, B., Frauscher, B., French, J., … Cross, J. H. (2025). Updated classification of epileptic seizures: Position paper of the International League Against Epilepsy. *Epilepsia.* https://doi.org/10.1111/epi.18338
11. Katyal, R. (2025). Classification and diagnosis of epilepsy. *CONTINUUM: Lifelong Learning in Neurology, 31*(1), 14–37. https://doi.org/10.1212/con.0000000000001519
12. Kannan, L., Jain, P., & Nayak, D. (2021). Role of Video-EEG in children. *The Indian Journal of Pediatrics, 88*(10), 1007–1016. https://doi.org/10.1007/s12098-020-03605-4
13. Cendes, F. (2013). Neuroimaging in investigation of patients with epilepsy. *CONTINUUM: Lifelong Learning in Neurology, 19,* 623–642. https://doi.org/10.1212/01.con.0000431379.29065.d3
14. Lippé, S., & Lassonde, M. (2004). Neuropsychological profile of intractable partial epilepsies. *Revue Neurologique,* 160(6–7), 585–592. https://pubmed.ncbi.nlm.nih.gov/15331960/
15. Zeng, K., Wang, X., Xi, Z., & Yan, Y. (2010). Adverse effects of carbamazepine, phenytoin, valproate and lamotrigine monotherapy in epileptic adult Chinese patients. *Clinical Neurology and Neurosurgery, 112*(4), 291–295. https://doi.org/10.1016/j.clineuro.2009.12.014

16. Nevitt, S. J., Sudell, M., Cividini, S., Marson, A. G., & Smith, C. T. (2022). Antiepileptic drug monotherapy for epilepsy: A network meta-analysis of individual participant data. *Cochrane Database of Systematic Reviews, 2022*(4). https://doi.org/10.1002/14651858.cd011412.pub4
17. Giorgi, L., Gomez, G., O'Neill, F., Hammer, A. E., & Risner, M. (2001). The tolerability of lamotrigine in elderly patients with epilepsy. *Drugs & Aging, 18*(8), 621–630. https://doi.org/10.2165/00002512-200118080-00006
18. Gouveia, F. V., Warsi, N. M., Suresh, H., Matin, R., & Ibrahim, G. M. (2024). Neurostimulation treatments for epilepsy: Deep brain stimulation, responsive neurostimulation and vagus nerve stimulation. *Neurotherapeutics, 21*(3), e00308. https://doi.org/10.1016/j.neurot.2023.e00308
19. Ramsay, R. E., Uthman, B. M., Augustinsson, L. E., Upton, A. R. M., Naritoku, D., Willis, J., Treig, T., Barolat, G., & Wernicke, J. F. (1994). Vagus nerve stimulation for treatment of partial seizures: 2. Safety, side effects, and tolerability. *Epilepsia, 35*(3), 627–636. https://doi.org/10.1111/j.1528-1157.1994.tb02483.x
20. Salanova, V., Witt, T., Worth, R., Henry, T. R., Gross, R. E., Nazzaro, J. M., Labar, D., Sperling, M. R., Sharan, A., Sandok, E., Handforth, A., Stern, J. M., Chung, S., Henderson, J. M., French, J., Baltuch, G., Rosenfeld, W. E., Garcia, P., Barbaro, N. M., … Bergen, D. (2015). Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy. *Neurology, 84*(10), 1017–1025. https://doi.org/10.1212/wnl.0000000000001334
21. Matias, C. M., Sharan, A., & Wu, C. (2019). Responsive neurostimulation for the treatment of epilepsy. *Neurosurgery Clinics of North America, 30*(2), 231–242. https://doi.org/10.1016/j.nec.2018.12.006
22. Roa, J. A., Marcuse, L., Fields, M., La Vega-Talbott, M., Yoo, J. Y., Wolf, S. M., McGoldrick, P., Ghatan, S., & Panov, F. (2023). Long-term outcomes after responsive neurostimulation for treatment of refractory epilepsy: A single-center experience of 100 cases. *Journal of Neurosurgery, 139*(5), 1463–1470. https://doi.org/10.3171/2023.2.jns222116
23. Milovanović, J. R., Janković, S. M., Milovanović, D., Zečević, D. R., Folić, M., Kostić, M., Ranković, G., & Stefanović, S. (2019). Contemporary surgical management of drug-resistant focal epilepsy. *Expert Review of Neurotherapeutics, 20*(1), 23–40. https://doi.org/10.1080/14737175.2020.1676733
24. Sperling, M. R., & Schnur, J. K. (2002). Temporal lobectomy. *Archives of Neurology, 59*(3), 482. https://doi.org/10.1001/archneur.59.3.482
25. Devlin, A. M. (2003). Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain, 126*(3), 556–566. https://doi.org/10.1093/brain/awg052
26. Van Empelen, R., Jennekens-Schinkel, A., Buskens, E., Helders, P., & Van Nieuwenhuizen, O. (2004). Functional consequences of hemispherectomy. *Brain, 127*(9), 2071–2079. https://doi.org/10.1093/brain/awh224
27. Auvin, S. (2025). Targeted therapies in epilepsies. *Revue Neurologique.* https://doi.org/10.1016/j.neurol.2025.04.003
28. Myers, K. A. (2023). SCN1A as a therapeutic target for Dravet syndrome. *Expert Opinion on Therapeutic Targets, 27*(6), 459–467. https://doi.org/10.1080/14728222.2023.2230364
29. Colasante, G., Lignani, G., Brusco, S., Di Berardino, C., Carpenter, J., Giannelli, S., Valassina, N., Bido, S., Ricci, R., Castoldi, V., Marenna, S., Church, T., Massimino, L., Morabito, G., Benfenati, F., Schorge, S., Leocani, L., Kullmann, D. M., & Broccoli, V. (2019). DCAS9-based *SCN1A* gene activation restores inhibitory interneuron excitability and attenuates seizures in Dravet syndrome mice. *Molecular Therapy, 28*(1), 235–253. https://doi.org/10.1016/j.ymthe.2019.08.018
30. Mukhtar, I. (2020). Inflammatory and immune mechanisms underlying epileptogenesis and epilepsy: From pathogenesis to treatment target. *Seizure, 82,* 65–79. https://doi.org/10.1016/j.seizure.2020.09.015
31. Lindefeldt, M., Eng, A., Darban, H., Bjerkner, A., Zetterström, C. K., Allander, T., Andersson, B., Borenstein, E., Dahlin, M., & Prast-Nielsen, S. (2019). The ketogenic diet influences taxonomic and functional composition of the gut microbiota in children with severe epilepsy. *NPJ Biofilms and Microbiomes, 5*(1). https://doi.org/10.1038/s41522-018-0073-2
32. Lum, G. R., Ha, S. M., Olson, C. A., Blencowe, M., Paramo, J., Reyes, B., Matsumoto, J. H., Yang, X., & Hsiao, E. Y. (2023). Ketogenic diet therapy for pediatric epilepsy is associated with alterations in the human gut microbiome that confer seizure resistance in mice. *Cell Reports, 42*(12), 113521. https://doi.org/10.1016/j.celrep.2023.113521
33. Arulsamy, A., Tan, Q. Y., Balasubramaniam, V., O'Brien, T. J., & Shaikh, M. F. (2020). Gut microbiota and epilepsy: A systematic review on their relationship and possible therapeutics. *ACS Chemical Neuroscience, 11*(21), 3488–3498. https://doi.org/10.1021/acschemneuro.0c00431
34. Pitkänen, A., Löscher, W., Vezzani, A., Becker, A. J., Simonato, M., Lukasiuk, K., Gröhn, O., Bankstahl, J. P., Friedman, A., Aronica, E., Gorter, J. A., Ravizza, T., Sisodiya, S. M., Kokaia, M., & Beck, H. (2016). Advances in the development of biomarkers for epilepsy. *The Lancet Neurology, 15*(8), 843–856. https://doi.org/10.1016/s1474-4422(16)00112-5
35. De Wachter, M., Schoonjans, A., Weckhuysen, S., Van Schil, K., Löfgren, A., Meuwissen, M., Jansen, A., & Ceulemans, B. (2023). From diagnosis to treatment in genetic epilepsies: Implementation of precision medicine in real-world clinical practice. *European Journal of Paediatric Neurology, 48,* 46–60. https://doi.org/10.1016/j.ejpn.2023.11.003

36. Alkhaldi, M., Joudeh, L. A., Ahmed, Y. B., & Husari, K. S. (2024). Artificial intelligence and telemedicine in epilepsy and EEG: A narrative review. *Seizure, 121,* 204–210. https://doi.org/10.1016/j.seizure.2024.08.024
37. AbuAlrob, M. A., Itbaisha, A., & Mesraoua, B. (2025). Unlocking new frontiers in epilepsy through AI: From seizure prediction to personalized medicine. *Epilepsy & Behavior, 166,* 110327. https://doi.org/10.1016/j.yebeh.2025.110327
38. Fattorusso, A., Matricardi, S., Mencaroni, E., Dell'Isola, G. B., Di Cara, G., Striano, P., & Verrotti, A. (2021). Pharmacoresistant epilepsy: An overview on existent and new emerging therapies. *Frontiers in Neurology, 12.* https://doi.org/10.3389/fneur.2021.674483
39. Knowles, J. K., Helbig, I., Metcalf, C. S., Lubbers, L. S., Isom, L. L., Demarest, S., Goldberg, E. M., George, A. L., Lerche, H., Weckhuysen, S., Whittemore, V., Berkovic, S. F., & Lowenstein, D. H. (2022). Precision medicine for genetic epilepsy on the horizon: Recent advances, present challenges, and suggestions for continued progress. *Epilepsia, 63*(10), 2461–2475. https://doi.org/10.1111/epi.17332
40. Kearney, H., Byrne, S., Cavalleri, G. L., & Delanty, N. (2019). Tackling epilepsy with high-definition precision medicine. *JAMA Neurology, 76*(9), 1109. https://doi.org/10.1001/jamaneurol.2019.2384