



Epilepsy

Jinwei Zhang^{1,2*} 

¹Hatherly Laboratories, Institute of Biomedical and Clinical Sciences, College of Medicine and Health, University of Exeter Medical School, Exeter EX4 4PS, UK

²State Key Laboratory of Bioorganic & Natural Products Chemistry, Research Center of Chemical Kinomics, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

***Correspondence:** Jinwei Zhang, Hatherly Laboratories, Institute of Biomedical and Clinical Sciences, College of Medicine and Health, University of Exeter Medical School, Exeter EX4 4PS, UK. j.zhang5@exeter.ac.uk

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Abstract

Epilepsy, a complex and widespread neurological disorder, has evolved in its understanding from ancient misconceptions to modern scientific advancements. This special issue highlights pivotal research and reviews on the mechanisms underlying epilepsy, innovative treatment strategies, and the psychosocial dimensions of living with this condition. Together, these contributions reflect the growing interdisciplinarity and depth in epilepsy research.

Keywords

Epilepsy, mechanisms, therapeutics, ion channels, social impact

Epilepsy, affecting over 50 million individuals globally (WHO), has historically been misunderstood [1], often seen through the lenses of superstition and stigma. Modern research has reframed epilepsy as a neurological disorder characterized by recurrent seizures due to abnormal brain activity [2]. While antiepileptic drugs (AEDs) effectively manage seizures for many patients, approximately 30% remain refractory to treatment, necessitating novel therapeutic approaches [3].

This special issue of Epilepsy within the journal of Exploration of Neuroscience features five original research articles and five comprehensive reviews, offering readers cutting-edge insights into epilepsy's pathophysiological mechanisms, emerging treatments, and psychosocial challenges. Below, we synthesize the key contributions.

Mechanisms and pathophysiology

Banerjee and Jirsa [2] provide a multiscale analysis of epilepsy, moving from cellular-level ion channel dysfunctions and astrocytic roles to whole-brain network dynamics. They emphasize the transformative potential of computational modeling for predicting seizures and personalizing treatments. Yamashita et al. [4] further illuminate the role of somatostatin-expressing inhibitory neurons in cortical layers 4/5, identifying mTORC1 signaling as a critical pathway in epileptogenesis. Their findings open avenues for targeted interventions.

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Epilepsy: Current Understanding and Future Directions

Global Impact

Affects over 50 million people worldwide
~30% of patients remain refractory to treatment

Mechanisms and Pathophysiology

- Ion channel dysfunction
- Astrocytic roles
- mTORC1 signaling pathway
- Oxidative stress

Psychosocial Aspects

- Persistent stigma
- Quality of life impacts
- Social support importance
- Public education needs

Therapeutic Advances

- Ketogenic diet variants
- Vagus nerve stimulation
- MRgLITT CC
- Targeted interventions

Future Research Priorities

- Computational modeling
- Personalized treatments
- Gene therapy potential
- Interdisciplinary approaches

Integrated Approach Needed

Combining research from molecular level to societal impact for comprehensive epilepsy management

Graphical abstract. Epilepsy: current understanding and future directions. The graphical abstract summarizes key aspects of epilepsy research and management. The global impact highlights the significant prevalence of epilepsy, affecting over 50 million individuals worldwide, with approximately 30% of patients resistant to current treatments. The “Mechanisms and Pathophysiology” section emphasizes underlying causes, including ion channel dysfunction, astrocytic roles, mTORC1 signaling, and oxidative stress. “Psychosocial Aspects” outline challenges such as persistent stigma, quality of life impacts, and the need for public education. Advances in therapy include ketogenic diet variants, vagus nerve stimulation, magnetic resonance-guided laser interstitial thermal therapy corpus callosotomy (MRgLITT CC), and targeted interventions. Future research priorities are outlined, focusing on computational modeling, personalized treatments, gene therapy, and interdisciplinary approaches. The conclusion stresses the need for an integrated approach combining molecular research with societal-level strategies for comprehensive epilepsy management

Žerovnik’s review [5] on progressive myoclonus epilepsies (PMEs) delves into molecular underpinnings like oxidative stress and mitochondrial dysfunction, with a focus on Unverricht-Lundborg disease. The exploration of gene therapy and autophagy-enhancing treatments underscores the potential for innovative therapeutic strategies.

Therapeutic advances

The ketogenic diet (KD), discussed by Vityala et al. [6], continues to show promise for refractory epilepsy, particularly in pediatric populations. This review evaluates variations of the KD, such as the modified Atkins diet, offering insights into balancing efficacy with patient compliance.

Gonzalez-Fernandez et al. [7] introduce a novel platform for transcutaneous vagus nerve stimulation (tVNS), showcasing its efficacy in reducing seizure frequency in drug-resistant epilepsy. Their pilot study underscores the importance of integrating artificial intelligence and patient-specific protocols for optimizing outcomes. Sheikh et al. [8] highlight the role of magnetic resonance-guided laser interstitial thermal therapy corpus callosotomy (MRgLITT CC) as a minimally invasive option for managing refractory epilepsy, particularly in complex pediatric cases.

Ricke’s study [9] examines adverse events (AEs) related to epilepsy following vaccinations. While most vaccines show no significant association, certain formulations exhibit elevated risks, particularly in infants and children with conditions like Dravet syndrome. These findings call for refined vaccination protocols and further investigations into potential manufacturing contaminants such as endotoxins.

Psychosocial and epidemiological perspectives

Yeni's review [10] focuses on the persistent stigma associated with epilepsy and its impact on quality of life. Despite medical advancements, societal misconceptions continue to hinder patients' social and psychological well-being. This is echoed in Walker and Peterson's longitudinal study [11], which underscores the importance of robust social support systems in improving outcomes for people with epilepsy (PWE).

Choque-Velasquez et al. [12] provide a comprehensive review of epilepsy in patients with arteriovenous malformations (AVMs). Their work highlights the prevalence of seizures, diagnostic challenges, and treatment options like microsurgical resection and stereotactic radiosurgery, emphasizing the need for tailored strategies to optimize outcomes.

Future directions

The contributions in this special issue highlight significant advancements in understanding epilepsy's complexities. Yet, they also underscore the need for continued interdisciplinary research—from elucidating molecular mechanisms to addressing societal challenges. The integration of computational models, targeted therapies, and public education campaigns offers a comprehensive pathway to enhancing the lives of individuals living with epilepsy.

By fostering dialogue and collaboration among researchers, clinicians, and policymakers, we can ensure that the next decade of epilepsy research is transformative. This special issue of *Exploration of Neuroscience* stands as a testament to the progress made and the potential yet to be realized in the field.

Abbreviations

KD: ketogenic diet

Declarations

Author contributions

JZ: Writing—original draft, Writing—review & editing.

Conflicts of interest

Jinwei Zhang is the Editorial Board Member and Guest Editor of *Exploration of Neuroscience* had no involvement in the decision-making or the review process of this manuscript.

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