

## Recent Advances in Epilepsy

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Epilepsy is a chronic neurological disorder where abnormal signals in nerve cells or neurons can result in strange sensations, altered behaviors and emotions, and in some cases, convulsions, loss of consciousness and muscle spasms. The exact underlying molecular and cellular mechanism of epilepsy, however, remains unclear. In this perspective, we outline the recent advances in the mechanism of epilepsy.

In the past few years, many important milestones have been achieved in our understanding of epilepsy. Oxidative stress is one of the possible mechanisms involved in epileptic seizures and evidence from both animal and human studies suggest that it may contribute to the onset and evolution of epilepsy. Biochemical and histological studies have shown that oxidative stress results in epileptogenesis in both neurons and astrocytes [1]. Some antioxidant drugs administered in rodents during an epileptic status, significantly decreased seizures [2]. Whereas Hu *et al.* reported that protein-rich extracts from *Bombyx batryticatus* have potential antiepileptic effects in PTZ-induced epilepsy by exerting anti-oxidative and anti-apoptotic effects through the PI3K/Akt signaling pathway [3]. These results highlight the possible pharmacological mechanisms associated with oxidative stress in epileptic seizures and how targeting oxidative stress may improve disease outcomes in a rat model of acquired epilepsy.

Many patients with mitochondrial disease also suffer from epileptic seizures. Epilepsy caused by mitochondrial genetic disorders leads to an insufficient supply of ATP due to nuclear or mitochondrial DNA mutations. The human neuropathological study shows that a deficiency of glutamine synthetase is an important pathogenic process for seizure onset in the brain, and astrocytes driven seizures in mitochondrial epilepsy [4]. Another pharmacological study showed that the activation of cannabinoid receptor 1 decreases the mitochondrial ATP levels which, in turn, open the potassium channel and contribute, at least in part, to its anticonvulsant effect [5]. Furthermore, post-treatment with the glucagon-like peptide-1 analogue inhibits mitochondrial stress induced by epileptic status [6]. A clearer understanding of the reciprocal relation between epilepsy and mitochondrial dysfunction is therefore critical in order to find the appropriate antiepileptic treatment. Based on evidences of mitochondrial and oxidative stress, antioxidants acting specifically in mitochondria might be beneficial in alleviating the epileptic seizures [7].

Ketogenic is a high fat, low carbohydrate, and controlled protein diet that has been used for the treatment of epilepsy in both children and adults, and is an alternative treatment for drug-resistant epilepsy. Recent evidence from human studies show that modified ketogenic diet therapies inhibit seizure frequency and severity with very few side effects [8]. In ketogenic mice, there was a significant reduction observed in epileptiform activity [9]. Genetic animal studies also revealed that the ketogenic diet regulates antioxidant catalase through PPAR $\gamma$ 2 activation, and that catalase may contribute to the ketogenic diet induced anti-seizure efficacy [10]. In another study, the ketogenic diet modulated mitochondrial function, decreased the formation of reactive oxygen species, increased the antioxidant capacity, and also prevented mutations in mitochondrial DNA [11]. These evidence suggest that ketogenic diet has a direct impact on improving mitochondrial function and decreasing oxidative stress in epilepsy [12, 13].

### CONCLUSION

In conclusion, in this perspective, we summarized the role of mitochondria-targeted antioxidant potential in epileptic seizure. Mitochondria-targeted antioxidant pathways may therefore be possible potential targets in ketogenic diet treatment for epilepsy. There is however still a need to further clarify mechanisms of mitochondria-targeted antioxidant action in the GABA-glutamate-glutamine cycle.

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**CONSENT FOR PUBLICATION**

Not applicable.

**FUNDING**

None.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest, financial or otherwise.

**ACKNOWLEDGEMENTS**

Declared none.

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