

## Review Article

# Epilepsy and Cognition

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**Abstract**

Many patients with epilepsy have some degree of cognitive impairment. The likelihood is increased for patients diagnosed with epilepsy during childhood. Active childhood epilepsy is associated with deficits in working memory, processing speed, and overall global cognitive impairment. In children, cognitive deficits translate into learning disabilities. Many factors influence cognitive function in patients with epilepsy. These include the epilepsy syndrome, the type and frequency of seizures, age of onset, frequency of spikes on electroencephalogram (EEG), and treatment with anti-epileptic drugs (AEDs). The cognitive impairment depends highly on the pathophysiology underlying the seizure disorder as well as the treatment that is used.

**ABBREVIATIONS**

AED: Anti-Epileptic Drugs; IED: Interictal Epileptiform Discharges; IGE: Idiopathic Generalized Epilepsy; JME: Juvenile Myoclonic Epilepsy; CAE: Childhood Absence Epilepsy; BRE: Benign Rolandic Epilepsy; TLE: Temporal Lobe Epilepsy; KD: Ketogenic Diet

**INTRODUCTION**

Epilepsy is one of the most common neurological disorders that affect people of all ages. Epileptic seizures result from abnormal, excessive or hypersynchronous neuronal activity in the brain [1]. Studies have shown that patients with epilepsy have some degree of cognitive impairment, including memory and attention deficits [1]. Epilepsy diagnosed in childhood can negatively affect the way the brain develops and matures leading to cognitive deficits [2]. Children with active epilepsy tend to have learning difficulty and poor academic performance. The exact nature and severity of the impairment depends on many factors including: the age of seizure onset, the location of the seizure focus, the nature of the seizure disorder, treatment with anti-epileptic drugs (AEDs), and psychosocial factors such as socioeconomic status and low self-esteem. Various epilepsy syndromes, frequency of spikes on EEG, and the use of AEDs are linked to cognitive impairment, whereas, non-pharmacological treatment such as the ketogenic diet has been shown to have neuroprotective effects on cognition [3].

**Epilepsy Syndromes**

The level of cognitive dysfunction is strongly associated with the underlying etiology and type of epilepsy syndrome. When critical functions are involved, the impact of epilepsy syndromes on cognition becomes concerning. Five most common epilepsy syndromes include idiopathic generalized epilepsy (IGE), juvenile myoclonic epilepsy (JME), childhood absence epilepsy (CAE), benign rolandic epilepsy (BRE), and temporal lobe epilepsy (TLE) [4].

Individuals with JME demonstrate frontal lobe dysfunction typically in areas including verbal and visual memory, verbal fluency, abstract reasoning, mental flexibility, and executive functions [4-6]. CAE arises from changes in the thalamocortical network. Individuals with CAE have deficits in global cognitive function, visual spatial function, and visual memory. Individuals with BRE have deficits in auditory-verbal learning, short-term memory, executive function, and fine motor activity [4]. TLE arises in the hippocampus and medial temporal lobe leading to anterograde memory loss; the greater the extent the of hippocampal atrophy, the more severe the memory impairment [5]. As one can see, epilepsy syndromes and their etiologies greatly affect cognitive function in a negative manner for people of all ages.

**Severity of Seizures**

Seizure severity is a crucial aspect of epilepsy [7]. Research has shown that frequent seizures can result in cognitive impairment. One particular study done by Thompson and Duncan found a strong relationship between cognitive decline and the frequency of generalized tonic-clonic seizures. Frequent complex partial seizures were also identified as a factor associated with cognitive decline. Cognitive decline was seen through worsening scores in tests of verbal learning, delayed recall, and semantic fluency [10]. Research has repeatedly shown that patients with intractable epilepsy, regardless of seizure type, may develop some form of cognitive impairment [7].

**Epileptiform Discharges**

Many patients with epilepsy develop some degree of cognitive or behavioral difficulties; however, in some cases when epilepsy is severe, the degree of psychomotor deterioration cannot be entirely explained by the underlying etiology or neurological comorbidities. In such cases, the condition is referred to as epileptic encephalopathy, and the cognitive impairment is believed to be due primary to the seizures or interictal epileptiform activity.

The concept of epileptic encephalopathy stems from the idea that frequent seizures or epileptiform discharges can interfere with normal neuronal physiology and cause disruption of various cognitive processes, such as plasticity, memory encoding, and language processing [8]. The presence of interictal epileptiform discharges (IEDs) is a strong diagnostic indicator of epilepsy requiring treatment with AEDs. Many studies have shown that treating IEDs results in decreased epileptiform activity or improved cognitive and behavioral functions.

### Ketogenic Diet

Alternative non-pharmacological treatment options, such as the ketogenic diet, have been successfully used to treat drug-resistant epilepsy. The KD consists of high-fat, medium protein, and low-carbohydrate foods [9]. Research has shown that effective implementation of KD results in strong neuroprotective effects with respect to social behavior and cognition. One particular study conducted in 2016, showed a positive cognitive and behavioral effect of the KD in children and adolescents with refractory epilepsy. These children showed increased mental alertness, improved attention, and improved cognition [10].

### Anti-Epileptic Drugs

Anti-epileptic drugs, old and new, have the potential to cause cognitive impairment. Likewise, polypharmacy can increase the likelihood of side effects such as cognitive deficits [11]. Older generation AEDs such as phenobarbital, carbamazepine, phenytoin and valproate have a greater chance of negatively affecting cognition yet may also be beneficial. Carbamazepine is associated with cognitive deficits in relation to processing speed and attention; however, it may also improve memory. Newer generation AEDs such as topiramate, levetiracetam, lamotrigine, and oxcarbazepine are, in general, better tolerated. Topiramate has been shown to be associated with poorer verbal fluency and working memory [4]. On the other hand, lamotrigine and levetiracetam have been shown to have positive effects on cognitive function in patients with epilepsy and may be beneficial in patients suffering from cognitive deficits. However, unless the drug is initiated through slow titration, cognitive side effects can be detrimental [11].

Conversely, the use of AEDs may also improve cognitive performance, especially in conditions associated with high frequency of interictal spikes [4]. It is critical to identify cognitive deficits that are potentiated by AED therapy. Once identified, modifications can be put in place to minimize the impact. The best ways to reduce the impact of AEDs on cognition are to avoid rapid titration, use the lowest AED dose, and choose slow release drugs [5]. Children, amongst all individuals, should be monitored closely for cognitive deficits while on AEDs. With developing nervous systems, they are extremely vulnerable to the long-term cognitive consequences associated with AEDs [4].

## CONCLUSION

Patients with epilepsy often experience cognitive dysfunction. Factors such as age of seizure onset, nature of the seizure type, and use of AED's contribute to the severity of the impairment. A study in the Journal of the International Neuropsychological Society showed that the most cognitively impaired were older individuals with the longest duration of epilepsy and prescribed polypharmacy [12]. In children, cognitive deficits may easily go undetected yet have a significant impact on quality of life, and have negative effects on daily functioning. Studies have repeatedly shown that multiple factors, including age of onset, location of seizure disorder, EEG findings, and severity, all have a major impact on cognition. Hence, early identification and intervention are crucial for each and every child diagnosed with epilepsy. Cognitive evaluation through brief screening tools or preferably comprehensive neuropsychological evaluation can be very helpful in identifying and monitoring cognitive deficits [2].

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