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"Seizure Profile And Cognition In Epilepsy"
A Review Of The Impact Of Seizure Profile On Cognitive Ability In Epilepsy

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Abstract

Irregular electrical activity in the brain is characteristic of epilepsy, a neurological condition that cognitively disables roughly 70-80% of those diagnosed. These cognitive challenges are subject to multiple influences, including the frequency of seizure occurrence, brain structure abnormalities, the effects of anti-epileptic medications, and individual patient traits. There is variation in the cognitive outcome depending on the type of epilepsy. For example, temporal lobe epilepsy tends to cause memory issues, while generalized epilepsies tend to present with milder impairments.

This review focuses on the tangled interaction of seizure frequency and brain network function on the decline of cognitive abilities related to epilepsy. Important pathological factors, such as those disrupting neurodegenerative processes, include damage to neurons inflicted by seizures, disconnection of brain networks, nervous system-derived inflammation, genetic influences, frequent biphasic wave activity during interictal periods, and sleep disruption, which weaken synaptic plasticity and memory.

Most of the cognitive deficits are linked to anti-epileptic drugs (AEDs). Although these drugs are essential for controlling seizures, especially in cases of polypharmacy or high dosage, their use tends to weaken cognition. Unlike older medications, modern anti-epileptic drugs have less of an effect on cognition. Additional risk factors include more severe medical co-morbidities like diabetes and hypertension, as well as lifestyle choices such as poor sleep and elevated stress levels, which can worsen cognitive decline.

In addressing such items, the modification of the patient's treatment in this case should focus heavily on the choice of medications, management of modifiable risk factors, and ongoing surveillance for biomarkers of cognitive impairment. The treatment plan should be constructed with each patient's multi-disciplinary team to better manage and ease the effects of epilepsy on cognition and quality of life.

Keywords: Epilepsy, Cognitive dysfunction, Anti-epileptic drugs (AEDs), Brain network disruption, Comorbid conditions, Neuroinflammation, Synaptic plasticity

Introduction

Epilepsy is a neurological disorder marked by abnormal electrical discharges in the brain, often leading to cognitive and behavioral impairment. Cognitive impairment is observed in 70-80% of

patients diagnosed with epilepsy, and it tends to precipitate with structural lesions, seizure activity, brain surgery, medication, and one's pre-existing cognitive reserve (Motamedi & Meador, 2003; Helmstaedter &Witt,2017). Further complicating the issue, different types of seizures have different impacts on deficits; for example, temporal lobe epilepsy has been associated with exacerbated loss of memory function, while generalized epilepsies tend to be less severe(Lenck-Saniti & Scott,2015)

The excessive, synchronized electrical activity in neurons, called a seizure, is either partial or generalized. Partial seizures typically begin at a specific cortical site and, over time, may spread to other parts of the brain; in contrast, generalized seizures do not require a specified starting point to initiate (Hoxhaj et al.,2023). During complex partial seizures, patients typically exhibit changes in conscious awareness, accompanied by mild eye and limb movements.

Epilepsy strikes approximately 50 million people worldwide, with increased prevalence among young children and individuals above the age of 60. The estimated prevalence is 6.38 per 1,000 for active epilepsy and 7.6 per 1,000 for lifetime epilepsy, with no remarkable difference by age or sex(Huff & Murr,2023). Cognitive deficits can affect memory, planning, and day-to-day functioning, ranging from mild to severe. It is treatment-resistant with more than 20 anti-seizure medications. Monotherapy is indicated with lamotrigine or carbamazepine for partial seizures, and sodium valproate for generalized seizures. Broad-spectrum AEDs, such as clobazam and brivaracetam, are effective for tonic-clonic seizures (Hoxhaj et al., 2023). Screening for cognitive impairment is necessary, as many patients are unaware of their deficits. Newly diagnosed patients, too, present with impairments in memory, psychomotor speed, and executive function, despite MRI abnormalities or normal use of AED(Piazzini et al.,2006; Novak et al.,2022).

AED can affect the feeling by changing the stimulation of neurons. Some of their effects are less than polytherapy, specifically affecting memory and attention(Quon et al.,2020; Ortinski & Meador,2004). The new AED is less impairing. Cognitive losses are correlated with seizure frequency and duration, with visual memory loss in 39.5% of patients, loss of attention in 23.7%, and common losses in 15.8%(Miller et al.,2016). Further investigation into biological markers of brain damage, including neuronal loss and sprouting, may provide deeper insight into the relationship between epilepsy severity and cognitive outcomes.

Pathophysiology Of Cognitive Impairment In Epilepsy

Etiological factor: 30-50% of cognitive deficits occur due to epilepsy(Holmes,2015; Novak et al.,2022). Genetic mutation (SCN1A, GABRA1, TSC1) interferes with ion channels and cortical growth, creating a hyperexcitable neural network. Acquired injuries like hypoxia or mesial temporal sclerosis can damage the hippocampus (memory-critical region)(Lodhi & Agrawal,2012).

Seizure-induced network disorder; Temporal lobe epilepsy reflects the hippocampus site cell instability, reducing theta rhythm synchronization (4-12 Hz) required for spatial memory(Holmes,2015; Novak et al.,2022). Hub Node distribution converts important network hubs to limbic areas, and integration between temporal and neocortical areas is impaired(Holmes,2015). Status epilepticus reduces long-term potentials (LTP) in CA1 Hippocampal Areas Via NMDA receptor dysfunction(Novak et al.,2022).

Interictal activity effect: Repeated interictal spikes disrupt the memory encoding into the left temporal lobe structures (Novak et al.,2022). It alters the sleep-type synaptic pruning (e.g., CSWS syndrome causes 85% spike-wave activity during slow sleep) induces hippocampal atrophy through chronic hyperexcitability(Novak et al.,2022; Lodhi & Agrawal,2012). Synaptic loss of plasticity; The memory circuit in the brain of epilepsy shows low neurogenesis and dendritic spine density. Excitotoxicity from the recurrent attacks may damage the glutamate receptor signaling pathway essential for learning(Lodhi & Agrawal,2012; Landi et al.,2018). Experimental models show that GABA-B receptor dysfunction in the Thalamocortical circuit exacerbates cognitive deficits related to epilepsy(Holmes & Lenck-Sanitini,2019).

West syndrome; Associate hyper-arrhythmia EEG pattern with visual processing deficit through metabolic intervention(Holmes & Lenck-

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Sanitini,2019). The ESES (Electric Status Epilepticus in sleep) disrupts sleep homeostasis, which causes the loss of language/motor function to be proportional to the spike load(Landi et al.,2018). Early seizure onset (<5 years) correlates with 3x greater cognitive decline due to interference with neurodevelopmental milestones(Samarasekera et al.,2015; Lodhi & Agarwal,2012).

While antiepileptic drugs contribute to cognitive effects, the primary pathophysiology involves synergistic interactions between etiological brain alterations, seizure-induced network reorganization, and sleep-activity disruptions(Holmes,2015; Novak et al.,2022; Lodhi & Agarwal,2012).

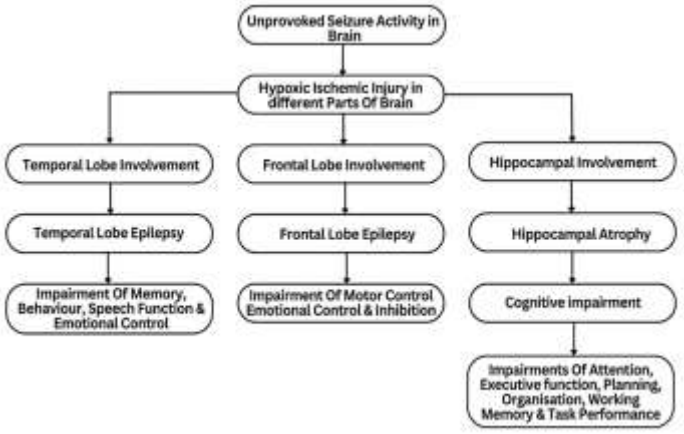

Figure 1: Pathophysiology of seizure-causing memory/cognitive impairment

Note: From "Cognitive impairment in adults with epilepsy: The relationship between subjective and objective assessments of cognition" by Samarasekera, S. R., Helmstaedter, C., & Reuber, M. (2015).Epilepsy & Behavior, 52(Pt A), 9–13. https://doi.org/10.1016/j.yebeh.2015.08.013

Pathogenesis Of Cognitive Impairment In Epilepsy

A complex interplay of seizure activity, brain network disruption, neuroinflammation, genetic factors, and drug effects generates cognitive loss in epilepsy.

The seizure-related neuronal damage causes excitotoxicity (excessive glutamate release), causing neuronal injuries. Hippocampal sclerosis, temporal lobe epilepsy (TLE), results in common memory deficits. Over time, neuronal apoptosis and synaptic loss deteriorate cognitive function(Dudek et al.,2021).

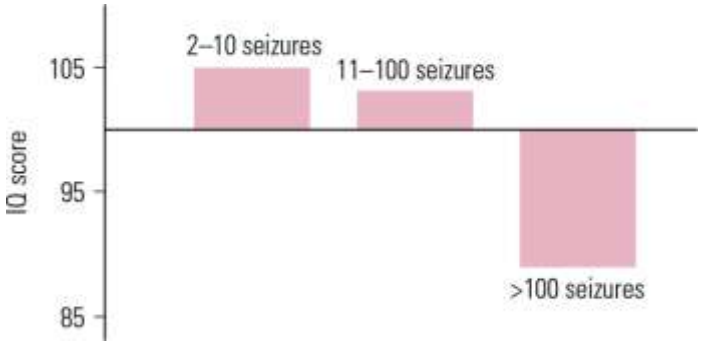

Figure 2: IQ score concerning the total number of lifetime seizures was analyzed in 94 adults who experienced secondarily generalized tonic-clonic seizures.

Note: From Correlates of Generalized Tonic-Clonic Seizures with Intellectual, Neuropsychological, Emotional, and Social Function in Patients with Epilepsy by Dodril,1986 https://doi.org/10.1111/j.1528-1157.1986.tb03559.x

Brain network dysfunction; Epileptic discharge disrupts general connectivity between cortical and subcortical areas. The default mode network (DMN) and hippocampus-prefrontal connectivity are particularly affected, leading to issues with attention and executive functions(Holmes & Lenck-Sanitini,2019).

Neuroinflammation and oxidative stress: epilepsy induces chronic neuroinflammation, characterized by microglial activation and cytokine release (e.g., IL-1β, TNF-α). It contributes to neuronal degeneration and cognitive deficits(Vezzani et al.,2020).

Genetic and epigenetic factors; some epilepsy-related genetic mutations (e.g., SCN1A, Grin2A, KCNQ2) are associated with intellectual disability. Epigenetic modifications, including DNA methylation, also contribute to cognitive decline(Busch et al.,2014).

The effect of anti-seizure drugs (ASMs); some ASMs, such as topiramate and phenobarbital, are known to be cognitively weak. However, new ASMs, such as levetiracetam, have more neutral or even protective effects(Ortinski & Meador,2004).

Seizure Triggers In The Aspect Of Cognitive Impairment

Cognitive loss in epilepsy is not only caused by the underlying pathological process but also by specific seizure triggers that can worsen cognitive function. These triggers in seizures contribute to brain

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dysfunction by increasing the frequency, leading to neuronal stress, and interrupting the brain network involved in cognition.

The status epilepticus (prolonged seizures 30 minutes) and persistent recurrent seizures induce morphological and functional brain changes, including low GABAergic inhibition, increased stimulation, and impaired synaptic plasticity (e.g., long-term potential deficiency. These changes disrupt the important hippocampus and neocortical network for memory and learning(Holmes,2015).

Lack of sleep reduces the seizure threshold, causing more frequent or severe seizures. Particularly reduces attention, processing speed, and memory consolidation in the hippocampus and prefrontal cortex. Studies show that lack of sleep slows with epilepsy, and the overall executive work deteriorates(Chan & Baldeweg,2022).

Stress activates the hypothalamic-pituitary-adrenal (HPA) axis and increases the level of cortisol, which can increase epileptic activity and reduce memory function. Chronic stress leads to hippocampal atrophy, reduces cognitive flexibility, and increases the risk of emotional deformity. Epilepsy patients often show deteriorating memory and executive deficits during the high-stress period(Jhaveri et al.,2023).

Medication non-adherence to the drug, such as irregular intake of anti-seizure medications (ASM), can result in uncontrolled seizures, leading to an increase in excitotoxicity and neuronal damage. Inconsistent seizure controls, worsening memory, attention, and processing speed deteriorate. Patients with poor drugs have a high cognitive burden, including difficulty in problem-solving and executive function(Mamo et al.,2024).

Poor diet and nutritional deficiency in essential nutrients (such as vitamin B6, folate, and omega-3 fatty acids) affect neurotransmitter balance and neuroprotection. The brain increases oxidative stress, which affects synaptic plasticity and leads to poor cognitive function. High dietary intake of processed sugars and low intake of antioxidants are associated with cognitive decline in epilepsy(Kim & Chao,2019).

Alcohol withdrawal and some recreational drugs (e.g., cannabis, cocaine) lower the seizure threshold and impair neuroplasticity. It can lead to memory deficits, impaired decisions, and a decrease in processing speed. Alcohol-related seizures are associated with more cognitive decline in epilepsy patients(Listabarth et al.,2022).

Hormonal changes (menstrual cycle, pregnancy, and thyroid laxity)- hormonal fluctuations affect neuronal stimulation, especially levels of estrogen and progesterone. Memory and mood regulation, especially in catamenial epilepsy (menstrual-related seizures), deteriorate. Women with epilepsy often report cognitive ups and downs related to their menstruation(Taubøll et al.,2015).

Environmental Triggers (Flashing Lights, Loud Noises, Overstimulation)-Certain external stimuli can trigger reflex seizures, disrupting cognitive function by overloading sensory processing networks. Causes attention deficits, confusion, and memory lapses after seizures. Photosensitive epilepsy is associated with worsened visual processing and working memory deficits(Harding & Jeavons,2022).

Surgery, especially the hippocampus and parahippocampal gyrus, is often resected in anterior temporal lobectomy (ATL), which is essential for memory. Left-sided resections, especially in language-dominant hemispheres, are particularly associated with verbal memory loss(Sherman et al.,2011).

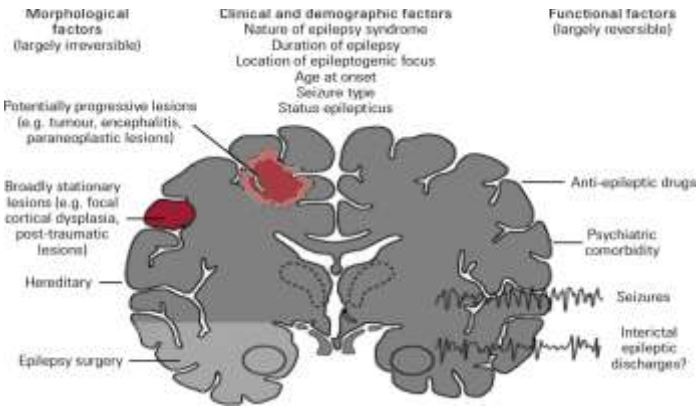

Figure 3: Factors affecting cognition in epilepsy**.**

Note: From "Chronic epilepsy and cognition" by Elger, Christian E et al.2004 The Lancet Neurology, Volume 3, Issue 11, 663 – 672 https://doi.org/10.1016/S1474-4422(04)00906-8

Comorbidities Influencing Seizure And Cognitive Function

Neuroinflammation and Autoimmune Disorders-Autoimmune epilepsy (AE) is linked to antibody-mediated neuronal damage, affecting cognitive

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function(Daimau & Graus,2018). Common Autoimmune Epilepsy Syndromes- Anti-NMDA receptor encephalitis: Leads to severe memory loss, confusion, and executive dysfunction(Wright et al.,2024).LGI1 encephalitis causes facio-brachial dystonic seizures and rapidly progresses to amnesia and executive dysfunction(Irani et al.,2013). Chronic low-grade neuroinflammation in epilepsy can worsen cognitive performance, even in the absence of overt seizures(Vezzani & Garanata,2005).

Psychiatric Comorbidities in Epilepsy, like Depression most common psychiatric comorbidity in epilepsy (approx. 20–55%). It impairs attention, processing speed, and memory also associated with reduced quality of life and poorer seizure control. Anxiety Disorders and Psychosis can also affect cognitive functioning(Kanner,2003; Tellex-Zento et al.,2007).

Metabolic and endocrine comorbidities, such as Diabetes Mellitus and Insulin Resistance-Epilepsy, patients have an increased risk of diabetes, particularly those on valproate or phenytoin(Li et al.,2021). Chronic hyperglycemia leads to hippocampal atrophy, affecting memory and learning(Moheet et al.,2015). Recurrent hypoglycemia in diabetic epilepsy patients worsens cognitive flexibility and attention(Biessels et al.,2014). Insulin dysfunction in epilepsy may play a direct role in seizure generation and cognitive impairment through disrupted neuronal metabolism.

Thyroid dysfunction, like Hypothyroidism, is common in epilepsy, especially in patients on carbamazepine, phenytoin, and valproate(Tamijani et al.,2015). Low thyroid hormone levels impair synaptic plasticity, reducing memory formation and attention(Bauer et al.,2008). Patients with both epilepsy and hypothyroidism exhibit more severe executive dysfunction than epilepsy patients without thyroid issues.

Obesity and Metabolic Syndrome. Epilepsy patients have a higher prevalence of obesity, partly due to AED-induced metabolic changes(Nazish,2023). Obesity-related inflammation affects the blood-brain barrier, impairing memory. Leptin resistance in obesity alters hippocampal function, worsening cognition(Forny et al.,2019). The ketogenic diet, used for epilepsy treatment, may reverse metabolic dysfunction and improve cognitive outcomes(Hallbook et al.,2012). Sleep Disorders and their cognitive consequences, like Obstructive Sleep Apnoea (OSA), affect 30–50% of epilepsy patients, with untreated OSA worsening cognitive impairment(Malow et al.,2003).

Sleep deprivation and fragmented sleep reduce attention span and working memory. Poor sleep exacerbates hippocampal atrophy, increasing the risk of dementia in epilepsy patients. Treating sleep apnoea with CPAP improves seizure control and cognitive function(Vaughn et al.,2012).

Antiepileptic Drugs (AEDs) and Cognitive Effects. Older AEDs like phenobarbital, topiramate, and benzodiazepines impair processing speed, attention, and memory(Drane & Meador,2002). Valproate and phenytoin increase the risk of cognitive slowing and executive dysfunction. Polytherapy with multiple AEDs is associated with greater cognitive impairment compared to monotherapy(Park & Kwon,2008).

The role of the gut-brain axis-AEDs affects gut microbiome composition, which may influence both cognitive function and seizure control(Dahlin & Prast, 2019). Microbiota alterations in epilepsy patients have been linked to neuroinflammation and cognitive decline. Probiotic supplementation is being explored as a method to counteract AED-induced cognitive effects(Olson et al.,2018).

Pharmacological Intervention-

The cognitive effect of Antiepileptic Drugs (AEDs) - AEDs modify neuronal stimulation by affecting ion channels, neurotransmitter release, or receptor functions. While their primary role is seizure control, some AEDs affect the feeling, while others have neutral or even cognitive-influential effects.

Many AEDs are there that negatively affect cognitive function: Phenobarbital is one of the oldest AEDs associated with sedation, memory dysfunction, and impaired attention(Meador et al.,2007). Topiramate: often causes word-finding difficulties, attention deficit, and slow processing speed(Lee et al.,2003). Benzodiazepines(e.g., Clonazepam, Diazepam) cause significant memory impairment, cognitive slowing, and sedation(Loring et al.,2007). Zonisamide: linked to psychomotor slowing and reduced attention span(Mula & Trimble,2009).

Some AEDs have a minimum effect on the feeling, or even cognitive results improve: Lamotrigine can have

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a pro-cognitive effect due to modulation of glutamatergic transmission(Seo et al.,2007). Levetiracetam does not impair cognition and may improve memory and attention(Helmstaedter et al.,2008).Lacosamide: Does not show significant cognitive effects(Ben-Menachem et al.,2007).

Pharmacological Strategies for Cognitive Enhancement-Acetylcholinesterase Inhibitors (AChEIs). Cholinergic dysfunction contributes to memory and learning impairments in epilepsy. AChEIs such as Donepezil, Rivastigmine, and Galantamine have been explored for cognitive deficits in epilepsy. Donepezil: Improves working memory and executive function in epilepsy patients(Correa et al.,2016). Rivastigmine has shown some benefit in enhancing cognitive processing speed(Aldenkamp et al.,2001).

Nootropics are substances that enhance cognition, neuroprotection, or neuroplasticity. Piracetam: Improves learning, memory, and neuroplasticity in epilepsy models(Dimond & Brouwers,1976). Aniracetam and Oxiracetam enhance synaptic transmission and memory function(Gouliaev & Senning,1994). NMDA Receptor Modulators-Memantine: An NMDA receptor antagonist that reduces excitotoxic damage and may enhance cognition(Sivakumar et al.,2022).

Non-Pharmacological Treatment-

Cognitive loss is a significant challenge for individuals with epilepsy, often affecting memory, attention, executive function, and processing speed. While pharmacological approaches can help, non-pharmacological intervention plays an important role in cognitive rehabilitation, offering alternative or complementary strategies without the ill effects of antiepileptic drugs (AEDs). It discovers evidence-based behavioral treatment, cognitive training, dietary intervention, neuromodulation, and lifestyle modifications, and aims to improve cognitive functions in epilepsy patients.

Cognitive behavior therapy (CBT) is widely used to address cognitive and emotional dysfunction in patients with epilepsy. Studies show that CBT helps: Increase memory and executive work through structured problem-solving and cognitive reorganization, and reduce anxiety related to epilepsy, which contributes to cognitive loss(Choudhary et al.,2024; Michaelis et al.,2020).

Cognitive rehabilitation therapy (CRT) includes structured exercises and strategies to improve specific cognitive skills such as meditation, memory, and problem-solving. A meta-analysis found that CRT improves oral memory and attention in epilepsy patients(Farina et al.,2015). CRT programs have shown significant improvement in working memory using computer-based cognitive training(Kurzbuch et al.2013).

Dietary intervention, such as the ketogenic diet (KD), is a high-fat, low-carbohydrate diet that has been widely studied for seizure control and cognitive improvement in epilepsy patients. Studies suggest that KD can increase cognitive function by improving mitochondrial energy metabolism(Ruskin et al.,2025). The use of long-term KD is associated with better memory and attention in children with epilepsy(Van et al.,2018). Modified Atkins diet (MAD): The modified Atkins diet (MAD) is a low-restrictive option for the ketogenic diet but still maintains ketosis, which is beneficial for cognitive function. Research shows that MAD improves executive functions and working memory in epilepsy patients(Sharma & Jain,2014).

Neuromodulation technology, such as transcranial magnetic stimulation (TMS), is a non-invasive brain stimulation technique used to enhance cognitive function in epilepsy patients. The study reports that repeated TMS (RTM) improves working memory and attention(Wei et al.,2016). Low-existent RTMs can reduce seizure frequency by increasing cognitive performance(Waltor et al.,2021).

Lifestyle modification: Physical activity has been linked to better cognitive function and neuroplasticity in epilepsy patients. Aerobic exercise enhances hippocampal function, which is important for memory. Resistance training is associated with improving executive function(Arida et al.,2018; Vancini et al.,2016).

Discussion

This review provides an intensive analysis of cognitive loss (CI) in epilepsy, emphasizing its multifactorial nature and adequately impact on the quality of life of patients. Nearly 70–80% of individuals with cognitive deficit disorder are affected by several factors, including sequential frequency, built-in etiology, anti-

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seizure medications (ASMs), and comorbid conditions. CI's pathophysiology in epilepsy is complex. This includes seizure-inspired neuronal damage, the disintegration of brain networks, neuroinflammation, genetic mutation, and adverse cognitive effects of ASM.

According to Dudek et al. (2021) & Dodril (1986), frequent seizures can cause excitotoxicity and neuronal injury, especially in memory-mating areas such as the hippocampus. Additionally, frequent intricate discharge memory reduces encoding and interferes with sleep-dependent synaptic shortening, which contributes to further cognitive decline.

Holmes (2015) emphasized that prolonged seizures (30 minutes or more), known as status epilepticus, and recurrent seizures can lead to both structural and functional changes in the brain and play an important role in the development of CI.

The study of Holmes(2015) and Novak et al.(2022) indicates that epilepsy discharges disrupt communication between cortical and subcortical regions, especially default mode networks (DMN) and Hippocampus-Prefrontal routes. These disruptions are associated with attention and loss of executive function.

Regarding pharmacological influences, Meador et al. (2007) reported that older-generation ASMs, such as phenobarbital and topiramate, significantly contribute to cognitive slowing. In contrast, newer ASMs like levetiracetam tend to have a more neutral or even protective cognitive profile (Lee et al., 2006). Moreover, polytherapy has been associated with a greater risk of cognitive impairment than monotherapy.

Li et al.(2021)discuss the role of comorbidities, such as diabetes mellitus (DM), hypertension (HTN), and autoimmune disorders, in worsening cognitive outcomes. For instance, chronic hyperglycemia in patients with diabetic epilepsy can lead to hippocampal atrophy, exacerbating cognitive decline.

According to Samarasekera et al.(2015), developmental considerations in epilepsy with early onset (before age 5) have a particularly detrimental effect on neurodevelopmental milestones, often resulting in more severe cognitive deficits than cases with later onset. Chan et al.(2011) and Jhaveri et al.(2023) both found that lifestyle-related factors such as sleep deprivation, stress, non-adherence to medication, poor nutrition, and hormonal fluctuations may further impair cognition by increasing seizure frequency and disrupting neural networks.

The purpose of future research is to identify reliable biomarkers for early identification and monitoring of cognitive loss and to develop neuroprotective therapy that targets seizure-related brain injury. Explore non-pharmacological interventions (e.g., cognitive training, neuromodulation, and lifestyle modifications) to support cognitive flexibility. Integrating these measures in regular clinical practice has the ability to reduce the cognitive burden of epilepsy, improve long-term functional results, and eventually increase the quality of life for patients and their families.

Conclusion

Cognitive loss remains one of the most important and disabling comorbidities in individuals with epilepsy. It originates from a complex difference of factors, including seizure frequency and duration, type, and severity of seizures, structural brain abnormalities, interrupted nervous connectivity, adverse effects of anti-epileptic drugs, and comorbid medical conditions. Of these, the seizure profile, which includes the age, frequency, type, duration, and severity of seizures, plays a central role in determining the boundary of cognitive decline. Evidence suggests that frequent and prolonged seizures, especially in childhood, are firmly associated with greater losses in memory, meditation, language, and executive functioning. In addition, there may be long-term disruption in the neural circuit required for learning and cognition of activity involving important brain areas such as the hippocampus and prefrontal cortex.

Effective management of epilepsy, therefore, requires a comprehensive and personal approach, not only focusing on the lack of seizures but also on preserving and enhancing cognitive function. Strategies should include aggressive management of initial diagnosis and seizures. A preference for monotherapy using a new ASM with fewer cognitive side effects. Regular cognitive assessment, especially in patients with early onset or drug-resistant epilepsy. Addressing variable lifestyle factors such as sleep hygiene, stress, and remedies. Multi-disciplinary care incorporating neurologists, neuropsychologists, and mental health professionals.

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Future research should aim to identify reliable biomarkers for early detection and monitoring of cognitive impairment and develop neuroprotective therapies that target seizure-related brain injuries. Explore nonpharmacological interventions to support cognitive ability.

Integrating these measures into routine clinical practice has the potential to reduce the cognitive burden of epilepsy, improve long-term functional outcomes, and ultimately enhance the quality of life for patients and their families.

Abbreviations

AEDs: Anti-epileptic drugs; **TLE:** temporal lobe epilepsy; **AE:** Autoimmune epilepsy; **OSA:** Obstructive sleep apnoea; **CBT:** Cognitive behavior therapy; **CRT:** Cognitive rehabilitation therapy; **KD:** ketogenic diet; **ATL:** anterior temporal lobectomy; **ASMs:** anti-seizure drugs;

LTP: long term potentials; **NMDA:** N-methyl-D-aspartate; **GABA:** Gamma aminobutyric acid; **AChEIs:** Acetylcholinesterase Inhibitors ;

Summary

This review looks at the complicated link between epilepsy and cognitive impairment, which affects 70-80% of patients. Cognitive issues, such as problems with memory, attention, and executive function, come from various factors, including how often and how long seizures occur, the underlying cause, anti-epileptic drugs (AEDs), and other health conditions. Temporal lobe epilepsy is especially linked to memory loss due to damage in the hippocampus, while generalized seizures generally have milder effects on cognition. Frequent and long seizures, particularly in early-onset epilepsy, lead to excitotoxicity, loss of neurons, and disrupted brain networks. This includes issues with the default mode network and the connection between the hippocampus and the prefrontal cortex, which damages learning and memory.

AEDs have a mixed role in treating epilepsy. Older medications like phenobarbital and topiramate can worsen cognitive problems, causing sedation, memory loss, and slower processing, especially when used in combination. Newer AEDs, such as levetiracetam and lamotrigine, tend to have fewer negative effects on cognition or may even protect cognitive function. Other health issues like diabetes, hypertension, thyroid problems, and obesity can make cognitive outcomes worse by causing neuroinflammation, hippocampal damage, and metabolic issues. Lifestyle factors such as lack of sleep, stress, poor nutrition, and not taking medication as prescribed can further increase seizures and cognitive decline. For example, lack of sleep reduces attention and memory, while stress raises cortisol levels, worsening damage to the hippocampus.

The article covers both drug and non-drug treatments. Acetylcholinesterase inhibitors like donepezil and nootropics like piracetam show potential for improving cognition. Non-drug methods such as cognitive behavioral therapy (CBT), cognitive rehabilitation therapy (CRT), and neuromodulation techniques like transcranial magnetic stimulation can enhance memory and attention. Diet changes, including the ketogenic and modified Atkins diets, can boost cognitive function by improving mitochondrial metabolism. Lifestyle changes, such as aerobic exercise and resistance training, support neuroplasticity and executive function.

The review stresses the importance of personalized, team-based treatment plans that focus on controlling seizures, assessing cognition, and managing lifestyle. Future research should aim to identify biomarkers for early detection of cognitive impairment and to develop neuroprotective treatments to reduce seizure-related brain damage. Combining these strategies in clinical practice could lessen the cognitive burden of epilepsy, improving long-term outcomes and overall quality of life for patients.

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