

Neurocognitive Effects of AEDs and Brain Connectivity in Drug-Resistant Epilepsy

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Introduction

Epilepsy, a neurological disorder characterized by recurrent seizures, affects millions worldwide, with significant implications for cognitive function and quality of life. In children, Anti Epileptic Drugs (AEDs) are the cornerstone of treatment, yet their use is often accompanied by cognitive side-effects, such as impaired memory, attention deficits and slowed processing speed, which can hinder development and academic performance. These effects are compounded by the underlying epilepsy pathology and seizure frequency, necessitating a careful balance between seizure control and cognitive preservation. Meanwhile, in Drug-Resistant Epilepsy (DRE), where seizures persist despite AED therapy, advanced neuroimaging techniques have revealed disruptions in brain connectivity, particularly in conditions like temporal lobe epilepsy. These connectome alterations, mapped through structural and functional networks, serve as biomarkers to predict surgical outcomes and elucidate the pathophysiology of DRE. Understanding the neurocognitive impacts of AEDs in pediatric patients and the connectome-based insights into DRE is critical for developing personalized treatment strategies that optimize both seizure management and cognitive outcomes, addressing the complex interplay between epilepsy, its treatment and brain function [1].

Description

The neurocognitive effects of AEDs in children with epilepsy are influenced by multiple factors, including the specific drug, dosage, polytherapy, epilepsy etiology and seizure activity. Older AEDs, such as phenobarbital, are associated with significant cognitive impairments, including reduced IQ, memory deficits and attention problems, due to their broad effects on neuronal excitability and GABAergic systems. In contrast, newer AEDs, like lamotrigine or levetiracetam, tend to have milder cognitive profiles, with some even showing neutral or beneficial effects on attention and mood. However, polytherapy common in severe cases increases the risk of cognitive side-effects, as drug interactions can amplify sedative or neurotoxic effects. The underlying epilepsy syndrome also plays a role; for instance, children with symptomatic epilepsies (e.g., due to brain lesions) are more vulnerable to cognitive deficits than those with idiopathic forms. Seizure frequency further exacerbates cognitive impairment, as recurrent seizures disrupt neural networks critical for learning and memory. Clinical studies emphasize that cognitive side-effects are not solely drug-related but result from a complex interplay of epilepsy-related factors, necessitating individualized treatment plans. Regular neuropsychological assessments are recommended to monitor cognitive function, allowing clinicians to adjust AED regimens, minimize

polytherapy, or explore non-pharmacological interventions like ketogenic diets to mitigate cognitive risks while maintaining seizure control.

In drug-resistant epilepsy, connectome-based neuroimaging has revolutionized the understanding of brain network disruptions and their role in treatment resistance. The connectome, a comprehensive map of structural and functional neural connections, is analyzed using techniques like Diffusion Tensor Imaging (DTI) and functional MRI (fMRI), particularly in temporal lobe epilepsy, a common DRE subtype. Studies reveal widespread network abnormalities, including reduced connectivity in the default mode network and altered white matter tracts, such as the uncinate fasciculus, which correlate with cognitive deficits and seizure propagation. These connectome alterations serve as biomarkers to predict outcomes of surgical interventions, such as temporal lobectomy, with patients showing more localized network disruptions often experiencing better postoperative seizure control. Machine learning models applied to connectome data further enhance predictive accuracy, identifying patterns of network reorganization that distinguish DRE from drug-responsive epilepsy. These findings suggest that DRE is not merely a focal disorder but a network-level pathology, with implications for cognitive function, as disrupted connectivity in regions like the hippocampus and prefrontal cortex underlies memory and executive impairments. Integrating connectome analysis into clinical practice could guide surgical planning, optimize candidate selection and inform novel therapies, such as neuromodulation, targeting aberrant networks to improve both seizure and cognitive outcomes [2].

Conclusion

The neurocognitive effects of AEDs in pediatric epilepsy and the connectome disruptions in drug-resistant epilepsy highlight the multifaceted challenges of managing this complex disorder. While AEDs are essential for seizure control, their cognitive side-effects, particularly in children, necessitate careful drug selection and monitoring to minimize developmental impacts. Concurrently, connectome-based insights into DRE reveal network-level abnormalities that serve as biomarkers for treatment resistance and surgical prognosis, offering a pathway to precision medicine. By integrating neuropsychological assessments with advanced neuroimaging, clinicians can develop personalized strategies that balance seizure management with cognitive preservation, ultimately improving quality of life for patients with epilepsy.

Acknowledgement

None.

Conflict of Interest

None.

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Received: 01 February, 2025, Manuscript No. jbr-25-168672; **Editor Assigned:** 03 February, 2025, PreQC No. P-168672; **Reviewed:** 15 February, 2025, QC No. Q-168672; **Revised:** 20 February, 2025, Manuscript No. R-168672; **Published:** 28 February, 2025, DOI: [10.38421/2684-4583.2025.8.294](https://doi.org/10.38421/2684-4583.2025.8.294)

References

1. Ijff, Dominique M. and Albert P. Aldenkamp. "Cognitive side-effects of antiepileptic drugs in children." *Handb Clin Neurol* 111 (2013): 707-718.
2. Lariviere, Sara andrea Bernasconi, Neda Bernasconi and Boris C. Bernhardt. "Connectome biomarkers of drug-resistant epilepsy." *Epilepsia* 62(2021): 6-24.

How to cite this article: Kristoffersen, Asger. "Neurocognitive Effects of AEDs and Brain Connectivity in Drug-Resistant Epilepsy." *J Brain Res* 8 (2025): 294.