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NEUROCOGNITIVE OUTCOMES ASSOCIATED WITH EARLY-ONSET EPILEPSY IN PEDIATRIC PATIENTS: A SYSTEMATIC REVIEW

DESFECHOS NEUROCOGNITIVOS ASSOCIADOS À EPILEPSIA DE INÍCIO PRECOCE EM PACIENTES PEDIÁTRICOS: UMA REVISÃO SISTEMÁTICA

DESENLACES NEUROCOGNITIVOS ASOCIADOS CON LA EPILEPSIA DE INICIO TEMPRANO EN PACIENTES PEDIÁTRICOS: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT: Early-onset epilepsy is a prevalent neurological disorder in childhood and may negatively affect neurocognitive development during critical periods of brain maturation. Factors such as age at seizure onset, epilepsy etiology, seizure burden, and antiseizure medication use may contribute to cognitive impairment. This systematic review aimed to analyze the available evidence on neurocognitive outcomes associated with early-onset epilepsy in pediatric patients and explore potential underlying mechanisms. A systematic literature review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. PubMed was searched using descriptors related to epilepsy, children, neurocognitive disorders, child development, and cognition. Studies published within the last 15 years in English or Portuguese were considered, and 10 studies were included in the qualitative synthesis. Methodological quality was assessed using the SANRA and EPHPP tools. Early-onset epilepsy was consistently associated with impairments in executive function, attention, memory, language, visuomotor skills, and psychomotor processing speed. Poorer outcomes were associated with earlier seizure onset, refractory epilepsy, epileptic encephalopathies, and structural or genetic etiologies. Early-onset epilepsy is strongly associated with persistent neurocognitive impairment, highlighting the importance of early assessment, multidisciplinary follow-up, and individualized interventions to optimize developmental outcomes.

Keywords: Child development. Epilepsy. Neurocognitive disorders.

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RESUMO: A epilepsia de início precoce é um dos transtornos neurológicos mais prevalentes na infância e pode afetar negativamente o desenvolvimento neurocognitivo durante períodos críticos da maturação cerebral. Fatores como idade, etiologia, carga epiléptica e uso de medicamentos antiepilépticos podem contribuir para o comprometimento cognitivo. Esta revisão teve como objetivo analisar as evidências disponíveis sobre os desfechos neurocognitivos associados à epilepsia de início precoce em pacientes pediátricos e explorar possíveis mecanismos envolvidos. Foi realizada uma revisão sistemática da literatura conforme as diretrizes Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020). A busca foi realizada na base PubMed, utilizando descritores relacionados à epilepsia, crianças, transtornos neurocognitivos, desenvolvimento infantil e cognição. Foram considerados estudos publicados nos últimos 15 anos, em inglês ou português, sendo incluídos 10 estudos na síntese qualitativa. A qualidade metodológica foi avaliada pelas ferramentas SANRA e EPHPP. A epilepsia de início precoce esteve associada a déficits em funções executivas, atenção, memória, linguagem, habilidades visuomotoras e velocidade de processamento psicomotor. Piores desfechos foram associados ao início precoce das crises, epilepsia refratária, encefalopatias epilépticas e etiologias estruturais ou genéticas. Esses achados reforçam a importância da avaliação precoce, do acompanhamento multidisciplinar e de intervenções individualizadas para otimizar o desenvolvimento neurocognitivo.

Palavras-Chave: Desenvolvimento infantil. Epilepsia. Transtornos neurocognitivos.

RESUMEN: La epilepsia de inicio temprano es uno de los trastornos neurológicos más prevalentes en la infancia y puede afectar negativamente el desarrollo neurocognitivo durante períodos críticos de maduración cerebral. Factores como la edad de inicio de las crisis, la etiología, la carga epiléptica y el uso de medicamentos antiepilépticos pueden contribuir al deterioro cognitivo. Esta revisión tuvo como objetivo analizar la evidencia disponible sobre los resultados neurocognitivos asociados con la epilepsia de inicio temprano en niños y explorar los posibles mecanismos involucrados. Se realizó una revisión sistemática de la literatura de acuerdo con las directrices Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020). La búsqueda se realizó en la base de datos PubMed, utilizando descriptores relacionados con epilepsia, niños, trastornos neurocognitivos, desarrollo infantil y cognición. Se consideraron estudios publicados en los últimos 15 años en inglés o portugués, incluyéndose 10 estudios en la síntesis cualitativa. La calidad metodológica se evaluó mediante las herramientas SANRA y EPHPP. La epilepsia de inicio temprano se asoció con déficits en funciones ejecutivas, atención, memoria, lenguaje, habilidades visuomotoras y velocidad de procesamiento psicomotor. Estos hallazgos destacan la importancia de la evaluación temprana, seguimiento multidisciplinario e intervenciones individualizadas para optimizar el desarrollo neurocognitivo.

Palabras clave: Desarrollo infantil. Epilepsia. Trastornos neurocognitivos.

INTRODUCTION

Epilepsy is a chronic non-communicable disease characterized by excessive electrical discharges in groups of cerebral neurons, resulting in recurrent epileptic seizures. These seizures consist of transient episodes of abnormal neuronal activity that can manifest with motor, sensory, autonomic, cognitive, or behavioral symptoms and may affect either a single cerebral hemisphere (focal seizure) or both hemispheres (generalized seizure). The diagnosis of epilepsy requires the presence of one of the following conditions: (1) at least two unprovoked

(or reflex) seizures occurring more than 24 hours apart; (2) one unprovoked (or reflex) seizure associated with a probability of recurrence similar to the general risk following two unprovoked seizures (≥60%) over the subsequent 10 years; or (3) the diagnosis of an epileptic syndrome (FISHER et al., 2014).

The etiology of epilepsy is heterogeneous and may involve structural, genetic, infectious, metabolic, immune, or unknown causes. Structural and acquired causes include traumatic brain injury (TBI), stroke, and brain malformations, while infectious causes include central nervous system infections such as meningitis and encephalitis. Epilepsy represents an important neurological condition among children and adolescents worldwide, with an estimated 18.15 million prevalent cases in this population in 2021 (KIM et al., 2026).

Given its epidemiological relevance and high prevalence during childhood, epilepsy is of particular concern not only because of recurrent seizures but also because of its impact on neurocognitive maturation. Children with epilepsy have up to a tenfold higher risk of intellectual disability (SORG et al., 2022) and frequently exhibit impairments in language, semantic functions, visuomotor skills, motor processing speed, and attention when compared with age-matched healthy individuals (KARRASCH et al., 2017; RATHOUZ et al., 2014).

These impairments may be influenced by several factors, including seizure frequency, interictal epileptiform discharges (AUVIN, 2022), the use of antiseizure medications (ASMs), such as Topiramate and Zonisamide (OPERTO et al., 2023), and the age at disease onset (SORG et al., 2022). Such impairments may significantly affect academic performance and have been reported in approximately 50% of children with epilepsy (JACKSON et al., 2012).

In this context, investigating the impact of early-onset epilepsy on neurocognitive development is essential, particularly because seizure onset during critical periods of brain maturation may interfere with neural plasticity (OPERTO et al., 2023). Early epileptic activity may also be associated with structural brain alterations, including reduced corpus callosum volume, disruption of white matter connectivity patterns, and decreased total brain volume (HERMANN et al., 2012; ZELKO et al., 2014).

Despite advances in the understanding of epilepsy, the cognitive consequences associated with this neurological disorder in the pediatric population, particularly in cases of early-onset epilepsy, remain incompletely characterized, and the available evidence is still limited and heterogeneous (JACKSON et al., 2012; KARRASCH et al., 2017; RATHOUZ et al., 2014). Furthermore, few studies have comprehensively synthesized the different cognitive

domains affected and the clinical factors associated with the severity of cognitive impairment in this population.

Therefore, this systematic review aimed to analyze and synthesize the available scientific evidence on neurocognitive outcomes associated with early-onset epilepsy in pediatric patients and identify the main clinical factors associated with these outcomes.

METHODS

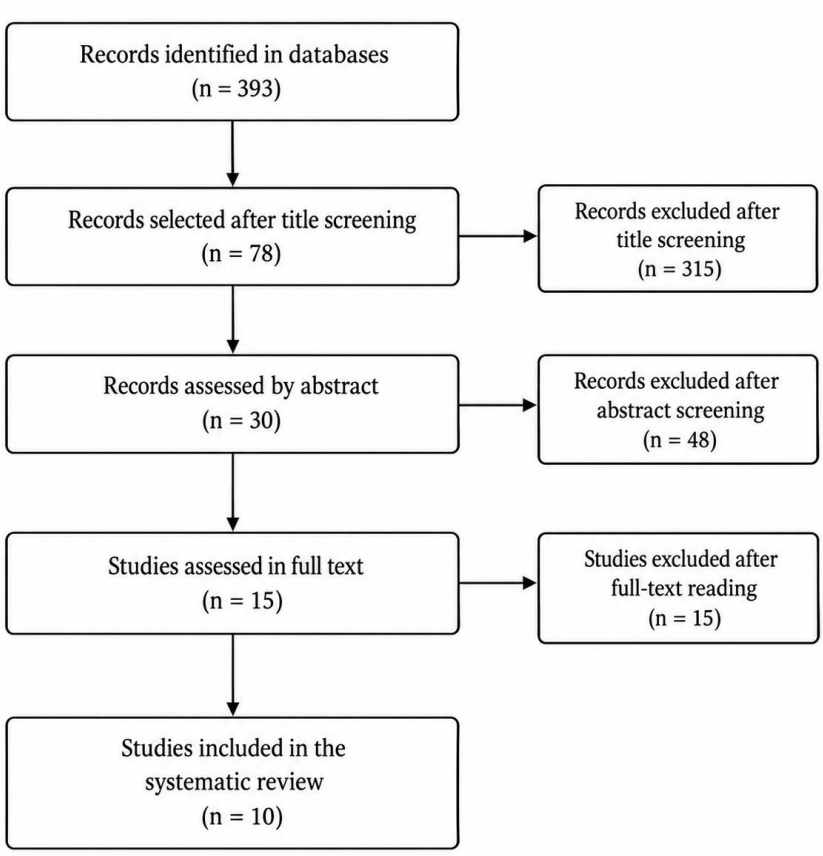
A systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to analyze the published evidence on the topic and synthesize the main findings regarding early-onset epilepsy and its impact on pediatric neurocognitive development. Additionally, this review sought to identify gaps in the current scientific literature and to improve the understanding of how this condition may affect long-term cognitive development in children. Accordingly, the following research question was established: What are the neurocognitive outcomes associated with early-onset epilepsy in pediatric patients, and which clinical factors are associated with these outcomes?

The literature search was performed in PubMed using a combination of Medical Subject Headings (MeSH) and free-text terms related to epilepsy, children, neurocognitive disorders, child development, and cognition, combined using the Boolean operators AND and OR. Articles published within the previous 15 years, available as free full-text publications, and written in either English or Portuguese were considered eligible. Studies involving children with early-onset epilepsy that reported data on neurocognitive development, cognition, learning, or other related cognitive outcomes were included. Duplicate publications, studies not directly related to the research topic, editorials, letters to the editor, and case reports were excluded.

Study selection was performed independently by five reviewers in successive stages, including title screening, abstract assessment, and full-text review of potentially eligible studies. Disagreements among the reviewers were resolved through discussion until a consensus regarding study inclusion or exclusion was reached. Initially, 393 articles were identified. After applying the predefined eligibility criteria, 78 studies remained for further assessment. Of these, 10 studies met the predefined eligibility criteria and were included in the qualitative synthesis (Figure 1).

Methodological quality and risk of bias were assessed according to the design of each included study. Narrative review articles were evaluated using the Scale for the Assessment of Narrative Review Articles (SANRA), which has a maximum score of 12 points. The included narrative reviews achieved scores ranging from 9 to 10, indicating satisfactory methodological quality, good thematic relevance, scientific coherence, and adequate theoretical foundation, despite some limitations in the description of the search strategy. Quantitative studies were assessed using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool and were classified as having moderate methodological quality, mainly because of the inherent limitations of observational study designs regarding control of confounding factors and blinding .

Figure 1. PRISMA 2020 flow diagram of the study identification, screening, eligibility, and inclusion process.



RESULTS

Characteristics of the Included Literature

The included literature comprised narrative reviews, prospective longitudinal studies, and population-based cohort studies (AUVIN, 2022; JACKSON et al., 2012; KARRASCH et al., 2017; OPERTO et al., 2023; RATHOUZ et al., 2014). The study populations consisted of pediatric patients with early-onset epilepsy, including infants, children, and adolescents, and were conducted primarily in North America and Europe (KARRASCH et al., 2017; OPERTO et al., 2023; SORG et al., 2022). The quantitative studies showed considerable variability in sample size, ranging from small clinical cohorts to population-based studies involving more than 142,000 participants (SORG et al., 2022) (Table 1).

Table 1. Characteristics and main contributions of the studies and reviews included in the evidence synthesis

Study	Type of study	Population / scope	Main topic evaluated	Main findings relevant to the review
Jackson et al. (2012)	Prospective/clinical study	Children with recent-onset epilepsy	Neuropsychological and academic performance	Early deficits in executive function, attention, psychomotor speed and academic performance
Rathouz et al. (2014)	Prospective longitudinal study	Children with new-onset epilepsy	Longitudinal cognitive outcomes	Cognitive deficits were detectable near diagnosis and remained relatively stable over follow-up
Karrasch et al. (2017)	Long-term cohort study	Individuals with childhood-onset epilepsy	Long-term neuropsychological outcomes	Persistent deficits in language, semantic and visuomotor functions
Sorg, von Kries & Borggraefe (2022)	Population-based longitudinal study	142,563 children	Cognitive impairment and age at epilepsy onset	Cognitive impairment was substantially more frequent among children with epilepsy,

				particularly with earlier onset
Hermann et al. (2012)	Narrative review	Children with new-onset epilepsy	Neuropsychological status and neurodevelopment	Cognitive difficulties may precede or accompany the first recognized seizure
Auvin (2022)	Narrative review	Pediatric epilepsy	Epilepsy, cognition and treatment	Cognitive outcomes influenced by epilepsy etiology, seizure burden, syndrome and antiseizure medication
Operto et al. (2023)	Mini-review	Children and adolescents with epilepsy	Cognitive impairment and neurodevelopment	Early onset, epileptic encephalopathies, drug resistance and treatment may influence neurocognitive outcomes

Neurocognitive Outcomes

Overall, the available evidence demonstrated a consistent association between early-onset epilepsy and neurocognitive impairment in children. Deficits in executive function, attention, and psychomotor processing speed were frequently reported among children with recent-onset epilepsy (JACKSON et al., 2012; RATHOUZ et al., 2014). Impairments in language, verbal memory, and visuomotor skills were also described in longitudinal follow-up studies (KARRASCH et al., 2017) (Table 2).

Furthermore, these impairments may be present from the early stages of the disease and, in some cases, even before the first recognized epileptic seizure, suggesting that pre-existing neurodevelopmental abnormalities and the epileptogenic process itself may contribute to impaired neurocognitive development (HERMANN et al., 2012; RATHOUZ et al., 2014).

In a longitudinal comparative study involving 142,563 children, 17.4% of those with epilepsy exhibited cognitive impairment, compared with 1.7% of healthy controls (SORG et

al., 2022). Several studies identified early seizure onset as one of the factors associated with poorer cognitive outcomes, particularly when epilepsy began before 5 years of age (AUVIN, 2022; OPERTO et al., 2023; SORG et al., 2022). Children whose seizures began during the first year of life showed significantly higher rates of intellectual disability and global developmental delay (AUVIN, 2022).

Prospective studies demonstrated that children with recent-onset epilepsy already present significant cognitive deficits at the time of diagnosis, particularly in attention, psychomotor processing speed, executive function, and mathematical learning (JACKSON et al., 2012; RATHOUZ et al., 2014). Longitudinal follow-up of up to 6 years showed that these impairments tend to remain relatively stable over time, with no significant evidence of spontaneous recovery (RATHOUZ et al., 2014). Moreover, long-term follow-up studies revealed that individuals with childhood-onset epilepsy continued to perform worse on language, semantic function, and visuomotor skill assessments even during middle adulthood (KARRASCH et al., 2017).

Table 2. Neurocognitive outcomes and factors associated with impairment

Study	Cognitive domains	Associated factors	Academic / functional impact
Jackson et al. (2012)	Attention, executive function, processing speed, memory	Recent-onset epilepsy	Learning and academic difficulties
Rathouz et al. (2014)	Attention, executive function, psychomotor speed, arithmetic	Early disease stage	Persistent academic difficulties
Karrasch et al. (2017)	Language, semantic function, visuomotor skills	Childhood-onset epilepsy, ongoing seizures	Long-term functional impact
Sorg et al. (2022)	Intellectual/cognitive impairment	Earlier age at seizure onset	Increased risk of intellectual disability
Hermann et al. (2012)	Neuropsychological development	Pre-existing neurodevelopmental abnormalities	Cognitive/academic difficulties may precede diagnosis

Auvin (2022)	Executive function, attention, memory and other domains	Etiology, seizure burden, ASMs	Academic and behavioral consequences
Operto et al. (2023)	Global cognition and neurodevelopment	Early onset, drug resistance, epileptic encephalopathies, ASMs	Developmental delay and functional impairment

Note: ASMs = antiseizure medications.

Factors Associated with Neurocognitive Impairment

Several studies identified earlier seizure onset as a factor associated with poorer cognitive outcomes, particularly when epilepsy began before 5 years of age (AUVIN, 2022; OPERTO et al., 2023; SORG et al., 2022). Children whose seizures began during the first year of life showed significantly higher rates of intellectual disability and global developmental delay (AUVIN, 2022).

Epileptic encephalopathies were consistently associated with the poorest neurocognitive outcomes. Syndromes such as West syndrome, Dravet syndrome, and Lennox–Gastaut syndrome showed a high frequency of severe cognitive impairment, behavioral disturbances, and global developmental delay, particularly among patients with frequent seizures and drug-resistant epilepsy (AUVIN, 2022; OPERTO et al., 2023). In a multicenter cohort of children with epilepsy during the first years of life, approximately 49% presented with global developmental disorder, while 36% developed drug-resistant epilepsy (OPERTO et al., 2023).

Antiseizure treatment was also evaluated in relation to cognitive outcomes. Polytherapy and the use of specific antiseizure medications, particularly Topiramate and Phenobarbital, were associated with a higher risk of cognitive impairment, especially affecting executive function and attention (AUVIN, 2022; OPERTO et al., 2023). Some studies also reported more favorable neurodevelopmental outcomes among children receiving monotherapy or early treatment initiation, particularly in more severe forms of epilepsy (AUVIN, 2022; OPERTO et al., 2023).

Academic and Functional Outcomes

In addition to neuropsychological deficits, academic difficulties and poor school performance were consistently reported across different pediatric epilepsy populations (AUVIN, 2022; JACKSON et al., 2012). Approximately 50% of children with epilepsy experienced poor academic performance, including learning difficulties, the need for special education services, and grade retention (AUVIN, 2022; JACKSON et al., 2012). Some studies reported that academic difficulties were present before the formal diagnosis of epilepsy (HERMANN et al., 2012).

Overall, there was broad agreement among the included studies regarding the association between early-onset epilepsy and neurocognitive impairment across multiple domains of child development. Nevertheless, some studies reported that children with self-limited or well-controlled epilepsies may exhibit milder cognitive deficits and better functional outcomes than those with drug-resistant epilepsy or epileptic encephalopathies (AUVIN, 2022; OPERTO et al., 2023). Despite this, even patients with less severe forms of epilepsy demonstrated a higher risk of academic difficulties and subtle cognitive impairments compared with the healthy pediatric population (JACKSON et al., 2012; KARRASCH et al., 2017; RATHOUZ et al., 2014).

DISCUSSION

The findings of the present study demonstrate that early-onset epilepsy is strongly associated with neurocognitive impairment across multiple domains of child development, with consequences that may emerge even before the clinical diagnosis and persist throughout life (AUVIN, 2022; HERMANN et al., 2012; JACKSON et al., 2012; KARRASCH et al., 2017; OPERTO et al., 2023; RATHOUZ et al., 2014; SORG et al., 2022). The available evidence revealed a high prevalence of deficits in executive function, attention, memory, language, psychomotor processing speed, and visuomotor skills, as well as a substantial impact on academic performance and overall functional outcomes (JACKSON et al., 2012; KARRASCH et al., 2017). These findings are particularly relevant because they indicate that, during childhood, epilepsy has the potential to directly interfere with essential processes involved in learning acquisition, autonomy, and social integration.

Among the factors most consistently associated with poor cognitive outcomes, age at seizure onset emerged as one of the strongest predictors. The longitudinal comparative study reported in the literature demonstrated that children with epilepsy had an approximately tenfold higher risk of cognitive impairment than healthy controls, with the risk increasing as the age at disease onset decreased (SORG et al., 2022). These findings are consistent with those of population-based studies and prospective cohorts reporting a higher prevalence of intellectual disability and global developmental delay among children whose seizures began before 5 years of age, particularly during the first year of life (AUVIN, 2022; OPERTO et al., 2023). This association may be explained by the fact that early childhood represents a critical period of brain maturation, during which synaptogenesis, myelination, and neural network reorganization occur intensively, rendering the developing brain particularly vulnerable to neurological insults (OPERTO et al., 2023).

The findings also indicated that epilepsy etiology appears to play an important role in the severity of neurocognitive outcomes. Children with structural, genetic, or metabolic epilepsies exhibited a higher frequency of intellectual disability and neurodevelopmental disorders than those with self-limited or well-controlled epilepsy syndromes (AUVIN, 2022; OPERTO et al., 2023). This observation is consistent with the current understanding that cognitive impairment often results not only from recurrent seizures but also from the underlying brain pathology itself. In developmental and epileptic encephalopathies, such as West syndrome, Dravet syndrome, and Lennox–Gastaut syndrome, this interaction becomes even more evident, as persistent epileptic activity acts as an additional contributor to cognitive and behavioral deterioration (AUVIN, 2022; OPERTO et al., 2023).

Another important finding was that cognitive and academic difficulties may be present even before the first recognized epileptic seizure (HERMANN et al., 2012; RATHOUZ et al., 2014). This observation expands the traditional understanding of epilepsy by suggesting that cognitive impairment and epileptic seizures may share common pathophysiological mechanisms, including genetic abnormalities, impaired synaptic plasticity, and neurodevelopmental disturbances (OPERTO et al., 2023). Consequently, in some patients, seizures do not represent the sole cause of cognitive deficits but rather constitute an additional manifestation of a broader underlying brain dysfunction.

Regarding the temporal course of cognitive impairment, prospective studies demonstrated that cognitive deficits are already detectable at the time of diagnosis and tend to

remain relatively stable throughout follow-up (JACKSON et al., 2012; RATHOUZ et al., 2014). These findings are consistent with those reported by Rathouz et al. (2014), who observed persistent cognitive deficits over a 6-year follow-up period, with no consistent evidence of spontaneous recovery. Furthermore, the long-term follow-up study by Karrasch et al. (2017) showed that individuals with childhood-onset epilepsy continued to perform worse on tests assessing language, semantic function, and visuomotor abilities even during middle adulthood. Together, these findings suggest that the neurocognitive consequences of childhood-onset epilepsy may extend beyond childhood and persist into adulthood.

Epileptic burden also appeared to be directly associated with neurocognitive prognosis. High seizure frequency, the presence of interictal epileptiform discharges, status epilepticus, and treatment resistance were all associated with an increased risk of global developmental delay and intellectual disability (AUVIN, 2022; OPERTO et al., 2023). A multicenter cohort described in the literature reported that approximately 36% of children developed drug-resistant epilepsy, whereas nearly 49% presented with global developmental disorder. These findings support the hypothesis that persistent epileptic activity exerts cumulative deleterious effects on the developing brain (OPERTO et al., 2023).

The impact of antiseizure treatment on cognition also deserves consideration. Although seizure control is essential for protecting brain development, certain antiseizure medications, including Topiramate, Zonisamide, and Phenobarbital, have been associated with poorer performance in attention, processing speed, and executive function (AUVIN, 2022; OPERTO et al., 2023). Conversely, monotherapy, gradual dose titration, and the use of the lowest effective dose were associated with more favorable cognitive outcomes (AUVIN, 2022; OPERTO et al., 2023). These findings have important clinical implications, reinforcing the need for individualized therapeutic strategies that consider not only seizure control but also the potential effects of treatment on neuropsychological functioning.

From a clinical perspective, the present findings highlight that the management of pediatric epilepsy should extend beyond seizure control. The high prevalence of academic difficulties, the need for educational support, and behavioral impairments emphasize the importance of multidisciplinary care involving neurologists, neuropsychologists, educational psychologists, speech-language pathologists, and school professionals (AUVIN, 2022; JACKSON et al., 2012; OPERTO et al., 2023). Early and periodic neuropsychological screening may facilitate the identification of subtle cognitive deficits and the implementation of

interventions aimed at minimizing academic and social impairments, thereby improving functional outcomes and quality of life.

From a research perspective, these findings underscore the need for further studies investigating early risk markers, underlying neurobiological mechanisms, and therapeutic strategies associated with reduced cognitive burden. Future longitudinal studies involving larger samples and standardized assessment tools may contribute to identifying potentially modifiable risk factors and determining the most effective interventions for preventing neurocognitive impairment. In addition, the development of specific protocols for cognitive monitoring may improve clinical practice and support more individualized patient management.

Several limitations should be considered when interpreting these findings. The included studies exhibited considerable heterogeneity regarding study design, sample characteristics, epilepsy subtypes, and cognitive assessment instruments, limiting direct comparisons across studies. The inclusion of narrative reviews alongside observational studies also limited the comparability of the evidence and may have introduced an additional risk of bias. It should also be acknowledged that the literature search was restricted to a single database and to free full-text articles published within the last 15 years, which may have limited the inclusion of potentially relevant studies.

Despite these limitations, the consistency of the findings across prospective cohorts, population-based studies, and long-term follow-up investigations strengthens the overall robustness of the available evidence. In summary, early-onset epilepsy represents a major risk factor for neurocognitive impairment, affecting multiple domains of cognitive development and negatively influencing academic performance, functional capacity, and quality of life (AUVIN, 2022; HERMANN et al., 2012; JACKSON et al., 2012; KARRASCH et al., 2017; OPERTO et al., 2023; RATHOUZ et al., 2014; SORG et al., 2022). Early identification of risk factors, together with the implementation of targeted therapeutic and rehabilitation strategies, is essential to minimize these adverse outcomes. Given the high prevalence of epilepsy during childhood and its potential to disrupt brain development during critical stages of maturation, advancing knowledge in this field remains fundamental to improving pediatric neurological care and developing novel strategies aimed at optimizing long-term neurocognitive outcomes in affected children.

CONCLUSION

The present systematic review analyzed the main neurocognitive outcomes associated with early-onset epilepsy in pediatric patients, demonstrating that this condition is strongly associated with impairments across multiple domains of child development. The studies included in this review consistently showed an association between early-onset epilepsy and deficits in executive function, attention, memory, language, psychomotor processing speed, and academic performance, with relevant consequences for academic and functional outcomes (AUVIN, 2022; HERMANN et al., 2012; JACKSON et al., 2012; KARRASCH et al., 2017; OPERTO et al., 2023; RATHOUZ et al., 2014; SORG et al., 2022).

The findings also demonstrated that factors such as early seizure onset, high epileptic burden, drug-resistant epilepsy, epileptic encephalopathies, and specific structural or genetic etiologies are associated with poorer cognitive outcomes (AUVIN, 2022; OPERTO et al., 2023; SORG et al., 2022). Furthermore, the evidence suggests that some neurocognitive abnormalities may be present even before the formal diagnosis of epilepsy, supporting the involvement of underlying neurobiological and neurodevelopmental mechanisms in the development of these deficits (HERMANN et al., 2012; RATHOUZ et al., 2014).

Another important finding was the persistence of cognitive impairment over time, indicating that the consequences of the disease may extend beyond childhood and persist into adulthood (KARRASCH et al., 2017; RATHOUZ et al., 2014). These findings emphasize the importance of early neuropsychological assessment and continuous multidisciplinary follow-up, focusing not only on seizure control but also on preserving cognitive development, academic achievement, and social integration.

In addition, the available evidence demonstrated that individualized therapeutic strategies, emphasizing the rational use of antiseizure medications and the early identification of risk factors, support the importance of individualized therapeutic strategies (AUVIN, 2022; OPERTO et al., 2023). In this context, recognizing pediatric epilepsy as a condition capable of profoundly affecting brain development highlights the need for more comprehensive clinical approaches tailored to the cognitive and functional needs of these patients.

Therefore, given the high prevalence of epilepsy during childhood and its potential to interfere with critical stages of brain maturation, a better understanding of the mechanisms underlying epilepsy-related neurocognitive impairment is essential for improving pediatric

neurological care and promoting better developmental prospects and quality of life for affected children.

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