NOOTROPIC AGENTS IN PEDIATRIC NEUROLOGY: CURRENT EVIDENCE, CLINICAL USE, AND SAFETY CONSIDERATIONS

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Abstract: Nootropic drugs are widely used in some clinical settings as adjunctive agents in the management and rehabilitation of pediatric neurological disorders. This review examines the pharmacological characteristics, proposed mechanisms of action, clinical applications, efficacy, and safety considerations of selected nootropic agents in pediatric neurology. Particular attention is given to piracetam, citicoline, hopantenic acid, phenibut, and pyritinol. The available literature suggests that the clinical effects of these agents vary considerably depending on the drug, neurological condition, age of the patient, and treatment context. Although some nootropics demonstrate potential effects on neuronal metabolism, neurotransmission, membrane function, and neuroplasticity, the available clinical evidence remains heterogeneous. Recent studies also indicate that the efficacy of individual agents cannot be generalized across different pediatric neurological disorders. Therefore, nootropic drugs should not be considered universal treatments and should be used only when clinically justified, with careful consideration of age-specific safety and potential adverse effects.

Keywords: Nootropic drugs, pediatric neurology, piracetam, citicoline, hopantenic acid, phenibut, pyritinol, neuroplasticity, cognitive function, neuroprotection.

Introduction

Pediatric neurology is a rapidly developing field of modern medicine that focuses on the diagnosis, treatment, and rehabilitation of neurological disorders occurring during childhood. Neurological conditions in children may result from a wide range of factors, including perinatal hypoxia and hypoxic-ischemic brain

injury, birth-related complications, genetic disorders, central nervous system infections, traumatic brain injury, metabolic abnormalities, and neurodevelopmental disorders. These conditions may affect cognitive, motor, behavioral, speech, and learning functions and, in some cases, may lead to long-term functional impairment. Nootropic drugs represent a heterogeneous group of pharmacological agents that have been traditionally described as substances capable of influencing cognitive functions and neuronal metabolism. The term “nootropic” was introduced by Corneliu E. Giurgea in 1972 in connection with the development of piracetam. Since then, numerous compounds with different pharmacological mechanisms have been classified as nootropics in various countries. These include agents proposed to influence neuronal membrane function, cellular energy metabolism, neurotransmission, neuroplasticity, or neuroprotective processes. However, the pharmacological properties and clinical indications of individual nootropic agents differ considerably, and the term “nootropic” does not represent a single pharmacological class with uniform mechanisms of action.

In pediatric neurology, some nootropic agents have been used as adjunctive therapies in children with cognitive or developmental difficulties, including selected cases of delayed psychomotor or speech development and during neurological rehabilitation. Proposed mechanisms include modulation of neuronal metabolism, effects on membrane phospholipid synthesis, changes in neurotransmitter activity, and potential support of neuronal plasticity. Nevertheless, evidence derived from experimental or pharmacological studies should not automatically be interpreted as evidence of clinical effectiveness in children. The clinical evidence concerning nootropic drugs in pediatric patients remains heterogeneous. Some individual agents have been investigated in specific neurological conditions, whereas for others, high-quality randomized controlled trials and long-term safety data are limited. Therefore, their potential benefits should be evaluated according to the specific drug, clinical indication, age of the

patient, treatment duration, safety profile, and quality of available evidence. In particular, nootropic agents should not be considered universal treatments for neurological or neurodevelopmental disorders.

Relevance

Neurological and neurodevelopmental disorders in children represent an important medical and social problem because they may affect cognitive development, speech, motor functions, behavior, learning ability, and the quality of life of children and their families. Perinatal hypoxia, hypoxic-ischemic brain injury, birth-related complications, central nervous system infections, traumatic brain injury, genetic and metabolic disorders may contribute to neurological impairment during childhood. Therefore, improving approaches to comprehensive treatment and rehabilitation of children with neurological disorders remains an important area of pediatric medicine.

Aim

The aim of this study is to analyze the pharmacological characteristics, proposed mechanisms of action, clinical applications, efficacy, and safety of selected nootropic drugs used in pediatric neurology, with particular attention to their potential role as adjunctive therapy in children with neurological and neurodevelopmental disorders.

Main part

Nootropic drugs are pharmacological agents traditionally used to influence cognitive functions and neuronal metabolic processes. Their pharmacological effects vary depending on their chemical structure and mechanism of action. Some nootropic agents may influence neuronal energy metabolism, neurotransmission, membrane function, and neuroplasticity. Piracetam is considered a classical nootropic agent and has been investigated for its effects on neuronal membrane function and cerebral metabolic processes. Citicoline is involved in phospholipid synthesis and has been studied for its potential role in maintaining neuronal membrane integrity. Hopantenic acid has pharmacological properties associated

with the GABAergic system and has traditionally been used in some pediatric neurological conditions. The proposed mechanisms of nootropic drugs include modulation of neuronal metabolism, support of cellular energy processes, and possible effects on synaptic plasticity. Some experimental studies have also suggested potential neuroprotective and antihypoxic properties of individual agents. However, pharmacological mechanisms observed in experimental models cannot automatically be considered evidence of clinical effectiveness. Therefore, clinical outcomes should be evaluated using appropriate human studies and evidence-based clinical data. In pediatric patients, pharmacological responses may differ from those observed in adults because of age-dependent physiological and pharmacokinetic characteristics. Consequently, the selection of a nootropic agent should take into account the child's age, diagnosis, neurological status, concomitant treatment, and potential risks. Nootropic therapy should therefore be considered individually rather than as a uniform treatment approach.

Nootropic drugs have traditionally been used in some countries as adjunctive therapy for selected neurological and neurodevelopmental conditions in children. The article describes their use in conditions associated with delayed psychomotor and speech development, cognitive difficulties, consequences of perinatal neurological injury, and rehabilitation after traumatic brain injury. In children with developmental delay, pharmacological treatment may be considered together with speech therapy, psychological support, special education, and other rehabilitation interventions. Following perinatal hypoxia or hypoxic-ischemic brain injury, comprehensive rehabilitation remains the principal therapeutic approach. Physiotherapy, therapeutic exercise, speech therapy, and developmental interventions may be combined according to the child's functional needs. Nootropic drugs, when considered, should only represent an adjunctive component rather than a replacement for rehabilitation. In attention-deficit/hyperactivity disorder, nootropic drugs are not considered first-line treatment in international clinical practice. Behavioral interventions, psychological support, parent

education, and approved pharmacological treatments are generally prioritized. Similarly, nootropic drugs are not established standard treatments for autism spectrum disorder. In children with cerebral palsy, treatment primarily focuses on motor rehabilitation, functional independence, communication, and management of associated problems.

The clinical efficacy of nootropic drugs remains heterogeneous and depends on the specific pharmacological agent and clinical condition. Some individual drugs have demonstrated potentially beneficial effects in selected studies, whereas evidence for other agents remains limited or inconsistent. Citicoline has been investigated for its potential neuroprotective and metabolic effects, including in pediatric neurological conditions. However, available clinical evidence does not support generalized conclusions regarding its effectiveness across all pediatric disorders. Piracetam has also been studied in relation to cognitive and neurological functions, but its clinical benefits should be interpreted according to the specific indication and quality of available evidence. Hopantenic acid is used in some countries, particularly within regional pediatric neurological practice, although internationally recognized high-quality evidence remains limited for several proposed indications. Phenibut requires particular attention because, in addition to its anxiolytic and GABA-related pharmacological effects, clinical literature has reported adverse effects associated with excessive use, dependence, withdrawal, and intoxication. Therefore, phenibut should not be presented as a routinely established pediatric nootropic therapy. Pyritinol has also been used historically as a nootropic agent, but its clinical application varies between countries and available evidence is not sufficient to support broad therapeutic claims. Safety assessment is especially important in children because adverse effects and drug interactions may have significant consequences.

The management of pediatric neurological disorders requires a comprehensive and multidisciplinary approach aimed at improving functional development and quality of life. Pharmacological treatment is only one component

of this approach. Depending on the underlying disorder, children may require physiotherapy, occupational therapy, speech and language therapy, psychological support, special education, and long-term developmental monitoring. Nootropic drugs have traditionally been incorporated into complex treatment programs in some clinical settings. Their proposed role is to support neuronal metabolism, cognitive functioning, or recovery processes. In children with developmental delay, any pharmacological intervention should be combined with appropriate developmental and educational rehabilitation. Following hypoxic-ischemic brain injury, rehabilitation should be individualized according to motor, cognitive, behavioral, and communication impairments. Similarly, after traumatic brain injury, treatment should focus on functional recovery and monitoring of cognitive symptoms. In children with epilepsy, additional caution is required because the effect of individual drugs on seizure control must be considered. Nootropic therapy should never replace established antiepileptic treatment or other evidence-based interventions. The potential value of a nootropic agent should therefore be evaluated as part of the overall treatment plan. This approach allows clinicians to avoid unnecessary pharmacological exposure while ensuring that potentially useful adjunctive interventions are considered when clinically appropriate.

From the perspective of evidence-based medicine, the therapeutic value of nootropic drugs should be determined by the quality and consistency of clinical evidence rather than by proposed pharmacological mechanisms alone. The available literature demonstrates substantial differences between individual nootropic agents, indications, study populations, and clinical outcomes. Some studies report potentially positive effects, while others show limited or inconclusive benefits. Therefore, the results obtained for one drug or one neurological condition should not automatically be extrapolated to other pediatric populations. Randomized controlled trials, systematic reviews, and long-term safety studies are particularly important for establishing the effectiveness of pharmacological interventions in children. Pediatric studies should also consider

age-specific pharmacokinetics, adverse effects, drug interactions, and long-term developmental outcomes. The current evidence does not support the use of nootropic drugs as universal treatments for pediatric neurological disorders. Instead, their use should be restricted to clinically justified situations in which the expected benefits outweigh potential risks. Treatment should be individualized according to the diagnosis, clinical severity, age of the child, and available evidence. Further well-designed clinical trials are required to clarify the efficacy and safety of individual nootropic agents. Such research may contribute to more accurate clinical recommendations and safer pharmacological decision-making in pediatric neurology.

Results

The analysis demonstrated that nootropic drugs represent a heterogeneous group of pharmacological agents with different mechanisms of action and clinical applications. The reviewed literature indicates that individual nootropic agents may influence neuronal metabolism, neurotransmission, membrane function, and neuroplasticity. However, the strength of clinical evidence varies considerably between individual drugs and neurological conditions. Piracetam and citicoline have been among the most frequently investigated agents, while hopantenic acid and pyritinol have been used predominantly in specific regional clinical practices. The available evidence suggests that the potential clinical effects of these agents depend strongly on the underlying neurological condition and characteristics of the pediatric population. Some studies have reported improvements in selected cognitive, neurological, or functional outcomes, whereas other investigations have failed to demonstrate statistically significant benefits. Recent clinical evidence concerning citicoline also indicates that its effects cannot be generalized to all pediatric neurodevelopmental disorders. In particular, clinical studies in children with autism spectrum disorder have not provided sufficient evidence to establish a consistent therapeutic benefit. The analysis also identified important safety considerations associated with certain agents. Phenibut, in particular, has been

associated with adverse effects, tolerance, dependence, withdrawal symptoms, and intoxication in the clinical literature. Therefore, its use in children requires particular caution. Overall, the results indicate that nootropic drugs may have a potential role as adjunctive agents in selected clinical situations, but current evidence does not support their universal use in pediatric neurology. The findings emphasize the importance of individualized treatment decisions, appropriate clinical indications, and continuous assessment of therapeutic benefits and potential risks.

Discussion

The findings of this review demonstrate that the clinical role of nootropic drugs in pediatric neurology remains controversial and requires careful interpretation of available evidence. Although several nootropic agents have demonstrated pharmacological effects on neuronal metabolism, membrane function, neurotransmission, and neuroplasticity, these mechanisms alone cannot be considered sufficient evidence of clinical effectiveness. The heterogeneity of published studies makes it difficult to establish uniform recommendations for the use of nootropic drugs in children. Differences in age, diagnosis, disease severity, treatment duration, outcome measures, and study methodology may contribute to the inconsistent findings reported in the literature. Citicoline provides an important example of this uncertainty, as its potential neuroprotective mechanisms have been investigated in different neurological conditions, while clinical benefits have not been consistently demonstrated in pediatric neurodevelopmental disorders. The safety profile of individual agents should also be considered when evaluating their potential clinical usefulness. Phenibut is particularly concerning because reports of dependence, withdrawal, intoxication, and other serious adverse effects limit its suitability as a routine pediatric therapy. These findings indicate that the risk-benefit ratio should be carefully assessed before prescribing any nootropic agent. In addition, nootropic treatment should not replace established rehabilitation strategies or evidence-based management of specific neurological disorders. For

children with developmental difficulties, cerebral palsy, autism spectrum disorder, or consequences of perinatal brain injury, multidisciplinary rehabilitation remains essential. Pharmacological interventions, when indicated, should complement rather than substitute these approaches. Therefore, the current evidence supports a selective and individualized approach to nootropic therapy rather than their routine or universal administration. Further large-scale randomized controlled trials with standardized clinical outcomes and long-term follow-up are required to determine the efficacy, safety, and appropriate indications of individual nootropic drugs in pediatric neurology.

Conclusion

The analysis of the available scientific literature indicates that nootropic drugs may have potential value as adjunctive pharmacological agents in selected areas of pediatric neurology. Their proposed effects include modulation of neuronal metabolism, neurotransmission, membrane function, and neuroplasticity. However, the clinical evidence supporting these effects remains heterogeneous and varies substantially between individual drugs and neurological conditions. Therefore, the pharmacological mechanism of a nootropic agent should not be considered sufficient evidence of its clinical efficacy. In pediatric patients, particular attention should be given to age-specific safety, potential adverse effects, drug interactions, and the limited availability of high-quality long-term clinical studies. The evidence currently available does not support the routine or universal use of nootropic drugs for pediatric neurological and neurodevelopmental disorders. Their administration should be individualized and considered only when there is a clear clinical indication and an appropriate assessment of the potential benefits and risks. Nootropic therapy should also not replace established rehabilitation, behavioral, educational, or disease-specific treatment strategies. Further well-designed randomized controlled trials involving adequately characterized pediatric populations are needed to determine the efficacy, safety, optimal indications, and long-term outcomes of individual nootropic agents. Such

evidence will help establish a more scientifically justified and clinically appropriate role for nootropic drugs in modern pediatric neurology.

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